

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number  
**WO 02/16965 A2**

(51) International Patent Classification<sup>7</sup>: **G01T**

[IL/IL]; 238 Hazait Street, 17940 Mitzpe Adi (IL). **ZILBERSTEIN**, Yoel [IL/IL]; 13 Zrubavel Street, 34671 Haifa (IL).

(21) International Application Number: **PCT/IL01/00638**

(74) Agent: **G. E. EHRLICH (1995) LTD.**; 28 Bezalel Street, 52521 Ramat Gan (IL).

(22) International Filing Date: 11 July 2001 (11.07.2001)

English

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language:

English

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(26) Publication Language:

English

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicant (*for all designated States except US*): **V-TARGET LTD.** [IL/IL]; 3 Ha'etgar Street, 39120 Tirat Hacarmel (IL).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **KIMCHY, Yoav** [IL/IL]; 8 Antwerpen Road, 34980 Haifa (IL). **AMRAMI, Roni** [IL/IL]; 37 Yarden Street, 20692 Yokneam (IL). **BOUSKILA, Yona** [IL/IL]; 44 Mikhmanim Street, 20106 Yokneam (IL). **ANTEBI, Udi** [IL/IL]; 30a Daphna Street, 27204 Kiryat Bialik (IL). **SIDORENKO, Nick** [IL/IL]; 4 Hamarva Street, 23393 Acre (IL). **BEN DAVID, Gal**



**WO 02/16965 A2**

(54) Title: RADIOACTIVE EMISSION DETECTOR EQUIPPED WITH A POSITION TRACKING SYSTEM AND UTILIZATION THEREOF WITH MEDICAL SYSTEMS AND IN MEDICAL PROCEDURES

(57) Abstract: A system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising (a) a radioactive emission detector; (b) a position tracking system being connected to and/or communicating with the radioactive emission detector; and (c) a data processor being designed and configured for receiving data inputs from the position tracking system and from the radioactive emission detector and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

1

RADIOACTIVE EMISSION DETECTOR EQUIPPED WITH A POSITION  
TRACKING SYSTEM AND UTILIZATION THEREOF WITH MEDICAL  
SYSTEMS AND IN MEDICAL PROCEDURES

5 FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to a radioactive emission detector equipped with a position tracking system. More particularly, the present invention relates to the functional integration of a radioactive emission detector equipped with a position tracking system as above with medical imaging modalities and/or with 10 guided minimally-invasive surgical instruments. The present invention is therefore useful for calculating the position of a concentrated radiopharmaceutical in the body in positional context of imaged portions of the body, which information can be used, for example, for performing an efficient 15 minimally invasive surgical procedure. The present invention further relates to a surgical instrument equipped with a position tracking system and a radioactive emission detector for fine *in situ* localization during resection and/or biopsy procedures, which surgical instrument is operated in concert with other aspects 20 of the invention.

The use of minimally invasive surgical techniques has dramatically 20 affected the methods and outcomes of surgical procedures. Physically cutting through tissue and organs to visually expose surgical sites in conventional "open surgical" procedures causes tremendous blunt trauma and blood loss. Exposure of internal tissues and organs in this manner also dramatically increases the risk 25 of infection. Trauma, blood loss, and infection all combine to extend recovery times, increase the rate of complications, and require a more intensive care and monitoring regiment. The result of such open surgical procedures is more pain and suffering, higher procedural costs, and greater risk of adverse outcomes.

In sharp contrast, minimally invasive surgical procedures cause little 30 blunt trauma or blood loss and minimize the risk of infection by maintaining the body's natural barriers to infection substantially intact. Minimally invasive surgical procedures result in faster recovery and cause fewer complications than

2

conventional, open, surgical procedures. Minimally invasive surgical procedures, such as laparoscopic, endoscopic, or cystoscopic surgeries, have replaced more invasive surgical procedures in all areas of surgical medicine. Due to technological advancements in areas such as fiber optics, micro-tool fabrication, imaging and material science, the physician performing the operation has easier-to-operate and more cost effective tools for use in minimally invasive procedures. However, there still exist a host of technical hurdles that limit the efficacy and increase the difficulty of minimally invasive procedures, some of which were overcome by the development of sophisticated imaging techniques. As is further detailed below the present invention offers a yet further advantage in this respect.

Radionuclide imaging is one of the most important applications of radioactivity in medicine. The purpose of radionuclide imaging is to obtain a distribution image of a radioactively labeled substance, e.g., a radiopharmaceutical, within the body following administration thereof to a patient. Examples of radiopharmaceuticals include monoclonal antibodies or other agents, e.g., fibrinogen or fluorodeoxyglucose, tagged with a radioactive isotope, e.g.,  $^{99\text{M}}\text{technetium}$ ,  $^{67}\text{gallium}$ ,  $^{201}\text{thallium}$ ,  $^{111}\text{indium}$ ,  $^{123}\text{iodine}$ ,  $^{125}\text{iodine}$  and  $^{18}\text{fluorine}$ , which may be administered orally or intravenously.

The radiopharmaceuticals are designed to concentrate in the area of a tumor, and the uptake of such radiopharmaceuticals in the active part of a tumor, or other pathologies such as an inflammation, is higher and more rapid than in the tissue that neighbors the tumor. Thereafter, a radiation emission detector, typically an invasive detector or a gamma camera (see below), is employed for locating the position of the active area. Another application is the detection of blood clots with radiopharmaceuticals such as ACUTECT from Nycomed Amersham for the detection of newly formed thrombosis in veins, or clots in arteries of the heart or brain, in an emergency or operating room. Yet other applications include radioimaging of myocardial infarct using agents such as

3

radioactive anti-myosin antibodies, radioimaging specific cell types using radioactively tagged molecules (also known as molecular imaging), etc.

The distribution image of the radiopharmaceutical in and around a tumor, or another body structure, is obtained by recording the radioactive emission of 5 the radiopharmaceutical with an external radiation detector placed at different locations outside the patient. The usual preferred emission for such applications is that of gamma rays, which emission is in the energy range of approximately 20-511 KeV. When the probe is placed in contact with the tissue, beta radiation and positrons may also be detected.

10 The first attempts at radionuclide "imaging" were in the late 1940's. An array of radiation detectors was positioned mechanically on a matrix of measuring points around the head of a patient. Alternatively, a single detector was positioned mechanically for separate measurements at each point on the matrix.

15 A significant advance occurred in the early 1950's with the introduction of the rectilinear scanner by Ben Cassen. With this instrument, the detector was scanned mechanically in a predetermined pattern over the area of interest.

The first gamma camera capable of recording all points of the image at one time was described by Hal Anger in 1953. Anger used a detector comprised 20 of a NaI(Tl) screen and a sheet of X-ray film. In the late 1950's, Anger replaced the film screen with a photomultiplier tube assembly. The Anger camera is described in Hal O. Anger, "Radioisotope camera in Hine GJ", Instrumentation in Nuclear Medicine, New York, Academic Press 1967, chapter 19. U.S. Patent No. 2,776,377 to Anger, issued in 1957, also describes such a radiation detector 25 assembly.

U.S. Patent No. 4,959,547 to Carroll et al. describes a probe used to map or provide imaging of radiation within a patient. The probe comprises a radiation detector and an adjustment mechanism for adjusting the solid angle through which radiation may pass to the detector, the solid angle being 30 continuously variable. The probe is constructed so that the only radiation

4

reaching the detector is that which is within the solid angle. By adjusting the solid angle from a maximum to a minimum while moving the probe adjacent the source of radiation and sensing the detected radiation, one is able to locate the probe at the source of radiation. The probe can be used to determine the  
5 location of the radioactivity and to provide a point-by-point image of the radiation source or data for mapping the same.

U.S. Patent No. 5,246,005 to Carroll et al. describes a radiation detector or probe, which uses statistically valid signals to detect radiation signals from tissue. The output of a radiation detector is a series of pulses, which are counted  
10 for a predetermined amount of time. At least two count ranges are defined by circuitry in the apparatus and the count range which includes the input count is determined. For each count range, an audible signal is produced which is audibly discriminable from the audible signal produced for every other count range. The mean values of each count range are chosen to be statistically  
15 different, e.g., 1, 2, or 3 standard deviations, from the mean of adjacent lower or higher count ranges. The parameters of the audible signal, such as frequency, voice, repetition rate, and/or intensity are changed for each count range to provide a signal which is discriminable from the signals of any other count range.

20 U.S. Patent No. 5,475,219 to Olson describes a system for detecting photon emissions wherein a detector serves to derive electrical parameter signals having amplitudes corresponding with the detected energy of the photon emissions and other signal generating events. Two comparator networks employed within an energy window, which define a function to develop an  
25 output, L, when an event-based signal amplitude is equal to or above a threshold value, and to develop an output, H, when such signal amplitude additionally extends above an upper limit. Improved reliability and accuracy is achieved with a discriminator circuit which, in response to these outputs L and H, derives an event output upon the occurrence of an output L in the absence of an output

H. This discriminator circuit is an asynchronous, sequential, fundamental mode discriminator circuit with three stable states.

U.S. Patent Nos. 5,694,933 and 6,135,955 to Madden et al. describe a system and method for diagnostic testing of a structure within a patient's body  
5 that has been provided with a radioactive imaging agent, e.g., a radiotracer, to cause the structure to produce gamma rays, associated characteristic x rays, and a continuum of Compton-scattered photons. The system includes a radiation receiving device, e.g., a hand-held probe or camera, an associated signal processor, and an analyzer. The radiation receiving device is arranged to be  
10 located adjacent the body and the structure for receiving gamma rays and characteristic X-rays emitted from the structure and for providing a processed electrical signal representative thereof. The processed electrical signal includes a first portion representing the characteristic X-rays received and a second portion representing the gamma rays received. The signal processor removes  
15 the signal corresponding to the Compton-scattered photons from the electrical signal in the region of the full-energy gamma ray and the characteristic X-ray. The analyzer is arranged to selectively use the X-ray portion of the processed signal to provide near-field information about the structure, to selectively use both the X-ray and the gamma-ray portions of the processed signal to provide  
20 near-field and far-field information about the structure, and to selectively use the gamma-ray portion of the processed signal to provide extended field information about the structure.

U.S. Patent No. 5,732,704 to Thurston et al. describes a method for identifying a sentinel lymph node located within a grouping of regional nodes at  
25 a lymph drainage basin associated with neoplastic tissue wherein a radiopharmaceutical is injected at the situs of the neoplastic tissue. This radiopharmaceutical migrates along a lymph duct towards the drainage basin containing the sentinel node. A hand-held probe with a forwardly disposed radiation detector crystal is maneuvered along the duct while the clinician  
30 observes a graphical readout of count rate amplitudes to determine when the

6

probe is aligned with the duct. The region containing the sentinel node is identified when the count rate at the probe substantially increases. Following surgical incision, the probe is maneuvered utilizing a sound output in connection with actuation of the probe to establish increasing count rate thresholds 5 followed by incremental movements until the threshold is not reached and no sound cue is given to the surgeon. At this point of the maneuvering of the probe, the probe detector will be in adjacency with the sentinel node, which then may be removed.

U.S. Patent No. 5,857,463 to Thurston et al. describes further apparatus 10 for tracking a radiopharmaceutical present within the lymph duct and for locating the sentinel node within which the radiopharmaceutical has concentrated. A smaller, straight, hand-held probe is employed carrying two hand actuatable switches. For tracking procedures, the probe is moved in an undulatory manner, wherein the location of the radiopharmaceutical-containing 15 duct is determined by observing a graphics readout. When the region of the sentinel node is approached, a switch on the probe device is actuated by the surgeon to carry out a sequence of squelching operations until a small node locating region is defined.

U.S. Patent Nos. 5,916,167 to Kramer et al. and 5,987,350 to Thurston 20 describe surgical probes wherein a heat-sterilizable and reusable detector component is combined with a disposable handle and cable assembly. The reusable detector component incorporates a detector crystal and associated mountings along with preamplifier components.

U.S. Patent No. 5,928,150 to Call describes a system for detecting 25 emissions from a radiopharmaceutical injected within a lymph duct wherein a hand-held probe is utilized. When employed to locate sentinel lymph nodes, supplementary features are provided including a function for treating validated photon event pulses to determine count rate level signals. The system includes a function for count-rate based ranging as well as an adjustable thresholding

7

feature. A post-threshold amplification circuit develops full-scale aural and visual outputs.

U.S. Patent Nos. 5,932,879 and 6,076,009 to Raylman et al. describe an intraoperative system for preferentially detecting beta radiation over gamma radiation emitted from a radiopharmaceutical. The system has ion-implanted silicon charged-particle detectors for generating signals in response to received beta particles. A preamplifier is located in proximity to the detector filters and amplifies the signal. The probe is coupled to a processing unit for amplifying and filtering the signal.

10 U.S. Patent No. 6,144,876 to Bouton describes a system for detecting and locating sources of radiation, with particular applicability to interoperative lymphatic mapping (ILM) procedures. The scanning probe employed with the system performs with both an audible as well as a visual perceptive output. A desirable stability is achieved in the readouts from the system through a signal 15 processing approach which establishes a floating or dynamic window analysis of validated photon event counts. This floating window is defined between an upper edge and a lower edge. The values of these window edges vary during the analysis in response to compiled count sum values. In general, the upper and lower edges are spaced apart a value corresponding with about four standard 20 deviations.

To compute these count sums, counts are collected over successive short scan intervals of 50 milliseconds and the count segments resulting therefrom are located in a succession of bins within a circular buffer memory. The count sum is generated as the sum of the memory segment count values of a certain 25 number of the bins or segments of memory. Alteration of the floating window occurs when the count sum either exceeds its upper edge or falls below its lower edge. A reported mean, computed with respect to the window edge that is crossed, is developed for each scan interval which, in turn, is utilized to derive a mean count rate signal. The resulting perceptive output exhibits a desirable

stability, particularly under conditions wherein the probe detector is in a direct confrontational geometry with a radiation source.

- U.S. Patent No. 5,846,513 teaches a system for detecting and destroying living tumor tissue within the body of a living being. The system is arranged to be used with a tumor localizing radiopharmaceutical. The system includes a percutaneously insertable radiation detecting probe, an associated analyzer, and a percutaneously insertable tumor removing instrument, e.g., a resectoscope. The radiation detecting probe includes a needle unit having a radiation sensor component therein and a handle to which the needle unit is releasably mounted.
- 5 The needle is arranged to be inserted through a small percutaneous portal into the patient's body and is movable to various positions within the suspected tumor to detect the presence of radiation indicative of cancerous tissue. The probe can then be removed and the tumor removing instrument inserted through the portal to destroy and/or remove the cancerous tissue. The instrument not only destroys the tagged tissue, but also removes it from the body of the being so that it can be assayed for radiation to confirm that the removed tissue is 10 cancerous and not healthy tissue. A collimator may be used with the probe to establish the probe's field of view.
- 15

The main limitation of the system is that once the body is penetrated, scanning capabilities are limited to a translational movement along the line of penetration.

An effective collimator for gamma radiation must be several mm in thickness and therefore an effective collimator for high energy gamma radiation cannot be engaged with a fine surgical instrument such as a surgical needle. On 20 the other hand, beta radiation is absorbed mainly due to its chemical reactivity after passage of about 0.2-3 mm through biological tissue. Thus, the system described in U.S. Patent No. 5,846,513 cannot efficiently employ high energy gamma detection because directionality will to a great extent be lost and it also 25 cannot efficiently employ beta radiation because too high proximity to the

9

radioactive source is required, whereas body tissue limits the degree of maneuvering the instrument.

The manipulation of soft tissue organs requires visualization (imaging) techniques such as computerized tomography (CT), fluoroscopy (X-ray 5 fluoroscopy), magnetic resonance imaging (MRI), optical endoscopy, mammography or ultrasound which distinguish the borders and shapes of soft tissue organs or masses. Over the years, medical imaging has become a vital part in the early detection, diagnosis and treatment of cancer and other diseases. In some cases medical imaging is the first step in preventing the spread of 10 cancer through early detection and in many cases medical imaging makes it possible to cure or eliminate the cancer altogether via subsequent treatment.

An evaluation of the presence or absence of tumor metastasis or invasion has been a major determinant for the achievement of an effective treatment for cancer patients. Studies have determined that about 30 % of patients with 15 essentially newly diagnosed tumor will exhibit clinically detectable metastasis. Of the remaining 70 % of such patients who are deemed "clinically free" of metastasis, about one-half are curable by local tumor therapy alone. However, some of these metastasis or even early stage primary tumors do not show with the imaging tools described above. Moreover often enough the most important 20 part of a tumor to be removed for biopsy or surgically removed is the active, i.e., growing part, whereas using only conventional imaging cannot distinguish this specific part of a tumor from other parts thereof and/or adjacent non affected tissue.

A common practice in order to locate this active part is to mark it with 25 radioactivity tagged materials generally known as radiopharmaceuticals, which are administered orally or intravenously and which tend to concentrate in such areas, as the uptake of such radiopharmaceuticals in the active part of a tumor is higher and more rapid than in the neighboring tumor tissue. Thereafter, a radiation emission detector, typically an invasive detector, is employed for 30 locating the position of the active area.

10

Medical imaging is often used to build computer models which allow doctors to, for example, guide exact radiation in the treatment of cancer, and to design minimally-invasive or open surgical procedures. Moreover, imaging modalities are also used to guide surgeons to the target area inside the patient's body, in the operation room during the surgical procedure. Such procedures may include, for example, biopsies, inserting a localized radiation source for direct treatment of a cancerous lesion, known as brachytherapy (so as to prevent radiation damage to tissues near the lesion), injecting a chemotherapy agent into the cancerous site or removing a cancerous or other lesions.

10       The aim of all such procedures is to pin-point the target area as precisely as possible in order to get the most precise biopsy results, preferably from the most active part of a tumor, or to remove such a tumor in its entirety on the one hand with minimal damage to the surrounding, non affected tissues, on the other hand.

15       However, in the current state of the prior art this goal is yet to be achieved, as most of the common imaging modalities such as fluoroscopy, CT, MRI, mammography or ultrasound demonstrate the position and appearance of the entire lesion with anatomical modifications that the lesion causes to its surrounding tissue, without differentiating between the non-active mass from 20 the physiologically active part thereof.

On the other hand, prior art radiation emission detectors and/or biopsy probes, while being suitable for identifying the location of the radiation site, they leave something to be desired from the standpoint of facilitating the removal or other destruction of the detected cancerous tissue with minimum invasion of the patient.

25       The combination of modalities, as is offered by the present invention, can reduce the margin of error in positioning such tumors. In addition, the possibility of demonstrating the position of the active part of a tumor superimposed on a scan from an imaging modality that shows the organ or 30 tumor, coupled with the possibility to follow a surgical tool in reference to the

<sup>11</sup>

afflicted area during a surgical procedure will allow for a more precise and controlled surgical procedures to take place, minimizing the aforementioned problems.

The present invention addresses these and other issues which are further elaborated hereinbelow, and offers the physicians and patients more reliable targeting, that in turn will result in less invasive and less destructive surgical procedures and less cases of mistaken diagnosis.

#### SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising (a) a radioactive emission detector; (b) a position tracking system being connected to and/or communicating with the radioactive emission detector; and (c) a data processor being designed and configured for receiving data inputs from the position tracking system and from the radioactive emission detector and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

According to another aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising (a) at least two radioactive emission detectors; (b) a position tracking system being connected to and/or communicating with at least two radioactive emission detectors; and (c) a data processor being designed and configured for receiving data inputs from the position tracking system and from the at least two radioactive emission detectors and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

According to still another aspect of the present invention there is provided a method for defining a position of a radioactivity emitting source in a system-of-coordinates, the method comprising the steps of (a) providing a radioactive emission detector being connected to or communicating with a

12

position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the radioactive emission detector in the system-of-coordinates , thereby defining the position of the radioactivity emitting source in the  
5 system-of-coordinates.

According to yet another aspect of the present invention there is provided a method for defining a position of a radioactivity emitting source in a system-of-coordinates, the method comprising the steps of (a) providing at least one radioactive emission detector being connected to or communicating with a  
10 position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the at least one radioactive emission detector in the system-of-coordinates, thereby defining the position of the radioactivity emitting source in the system-of-coordinates.

15 According to yet another aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising (a) a radioactive emission detector; (b) a position tracking system being connected  
20 to and/or communicating with the radioactive detector; and (c) a data processor being designed and configured for (i) receiving data inputs from the position tracking system and from the radioactive emission detector; (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; and (iii) projecting the position of the radioactivity emitting source onto the  
25 second system-of-coordinates.

According to still another aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising (a) at least two radioactive emission detectors; (b) a position  
30

13

tracking system being connected to and/or communicating with the at least two radioactive emission detectors; and (c) a data processor being designed and configured for (i) receiving data inputs from the position tracking system and from the at least two radioactive emission detectors; (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; and (iii) projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

According to still another aspect of the present invention there is provided a method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the method comprising the steps of (a) providing a radioactive emission detector being connected to or communicating with a position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the radioactive emission detector in the first system-of-coordinates, thereby defining the position of the radioactivity emitting source in the first system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

According to an additional aspect of the present invention there is provided a method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the method comprising the steps of (a) providing at least one radioactive emission detector being connected to or communicating with a position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the at least one radioactive emission detector in the first system-of-coordinates, thereby defining the position of the radioactivity emitting source in the first system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

14

According to yet an additional aspect of the present invention there is provided a system for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the system comprising (a) a two-dimensional (projectional or cross-sectional) or a three-dimensional (consecutive cross-sectional) imaging modality being connected to and/or communicating with a first position tracking system for calculating the position of the body component in a first system-of-coordinates; (b) a radioactive emission detector being connected to and/or communicating with a second position tracking system for tracking a 5 position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and (c) at least one data processor being designed and configured for receiving data inputs from the three-dimensional imaging modality, the first position tracking system, the radioactive emission detector and the second position tracking system and calculating the position of 10 the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

According to yet an additional aspect of the present invention there is provided a method for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the method comprising the steps of (a) providing a two-dimensional or a three-dimensional imaging modality being connected to and/or communicating with a first position tracking system and calculating the position of the body component in a first system-of-coordinates; (b) providing a radioactive emission detector being connected to and/or communicating with a 20 second position tracking system and tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and (c) receiving data inputs from the three-dimensional imaging modality, the first position tracking system, the radioactive emission detector and the second position tracking system and calculating the position of 25 the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

According to still an additional aspect of the present invention there is provided a system for performing an intrabody surgical procedure on a 5 radiopharmaceutical uptaking portion of a body component within a subject, the system comprising (a) a radioactive emission detector being connected to and/or communicating with a first position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a first system-of-coordinates; (b) a surgical instrument being connected to and/or 10 communicating with a second position tracking system for tracking a position of the surgical instrument in a second system-of-coordinates; and (c) at least one data processor being designed and configured for receiving data inputs from the first position tracking system, the radioactive emission detector and the second position tracking system and for calculating the position of the surgical 15 instrument and the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

According to a further aspect of the present invention there is provided a method for performing an intrabody surgical procedure on a radiopharmaceutical uptaking portion of a body component within a subject, the 20 method comprising the steps of (a) providing a radioactive emission detector being connected to and/or communicating with a first position tracking system and tracking a position of the radiopharmaceutical uptaking portion of the body component in a first system-of-coordinates; (b) providing a surgical instrument being connected to and/or communicating with a second position tracking system and tracking a position of the surgical instrument in a second system-of-coordinates while performing the intrabody surgical procedure; and 25 (c) receiving data inputs from the first position tracking system, the radioactive emission detector and the second position tracking system and calculating the position of the surgical instrument and the radiopharmaceutical uptaking portion

16

of the body component in a common system-of-coordinates while performing the intrabody surgical procedure.

According to further features in preferred embodiments of the invention described below, the second system-of-coordinates serves as the common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in the first system-of-coordinates is projected onto the second system-of-coordinates.

According to still further features in the described preferred embodiments the first system-of-coordinates serves as the common system-of-coordinates and therefore the position of the surgical instrument in the second system-of-coordinates is projected onto the first system-of-coordinates.

According to still further features in the described preferred embodiments the second system-of-coordinates, the first system-of-coordinates and the common system-of-coordinates are a single system-of-coordinates.

According to still further features in the described preferred embodiments the first system-of-coordinates, the second system-of-coordinates and the common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in the second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in the first system-of-coordinates are both projected onto the common system-of-coordinates.

According to still further features in the described preferred embodiments the first position tracking system and the second position tracking system are a single position tracking system.

According to still further features in the described preferred embodiments an image presentation device serves for visual co-presentation of the position of the surgical instrument and the radiopharmaceutical uptaking portion of the body component.

17

According to still further features in the described preferred embodiments the radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radioactive emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector, such as a gamma camera employed in nuclear imaging.

According to still further features in the described preferred embodiments the first and the second position tracking systems may include, but are not limited to, any combination of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical (e.g., optical encoder) based position tracking system.

According to still further features in the described preferred embodiments the surgical instrument may include, but is not limited to, any combination of laser probe, cardiac catheter, angioplasty catheter, endoscopic probe, biopsy needle, ultrasonic probe, fiber optic scopes, aspiration tubes, laparoscopy probe, thermal probe and suction/irrigation probe.

According to still further features in the described preferred embodiments the radiopharmaceutical may include, but is not limited to, <sup>131</sup>I, <sup>67</sup>Ga (which may be administered as Ga-citrate), <sup>99m</sup>Tc methoxyisobutyl isonitrile, <sup>201</sup>TlCl, <sup>18</sup>F-fluorodeoxyglucose, <sup>125</sup>I-fibrinogen and <sup>111</sup>In-octreotide, to name a few.

According to still further features in the described preferred embodiments the two- or three-dimensional imaging modality is connected to and/or communicating with a third position tracking system and is used for calculating the position of a body component in a third system-of-coordinates.

According to still further features in the described preferred embodiments data inputs are received from the two- or three-dimensional

18

imaging modality and the third position tracking system and are used for calculating the position of the surgical instrument and the position of the radiopharmaceutical uptaking portion of a body component and the position of the body component in a common system-of-coordinates.

5 According to still further features in the described preferred embodiments the first position tracking system, the second position tracking system and the third position tracking system are a single position tracking system.

10 According to still further features in the described preferred embodiments the position of the surgical instrument, the radiopharmaceutical uptaking portion of the body component and the body component are co-represented by a visual presentation device.

15 According to still further features in the described preferred embodiments each of the first, the second and the third position tracking system is independently selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

20 According to still further features in the described preferred embodiments the second system-of-coordinates serves as the common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in the first system-of-coordinates and the position of the body component in the third system-of-coordinates are projected onto the second system-of-coordinates.

25 According to still further features in the described preferred embodiments the first system-of-coordinates serves as the common system-of-coordinates and therefore the position of the surgical instrument in the second system-of-coordinates and the position of the body component in the third system-of-coordinates are projected onto the first system-of-coordinates.

19

According to still further features in the described preferred embodiments the third system-of-coordinates serves as the common system-of-coordinates and therefore the position of the surgical instrument in the second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in the first system-of-coordinates are projected onto the third system-of-coordinates.

According to still further features in the described preferred embodiments the second system-of-coordinates, the first system-of-coordinates, the third system-of-coordinates and the common system-of-coordinates are a single system-of-coordinates.

According to still further features in the described preferred embodiments the second system-of-coordinates, the first system-of-coordinates, the third system-of-coordinates and the common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in the second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in the first system-of-coordinates and the position of the body component in the third system-of-coordinates are all projected onto the common system-of-coordinates.

According to another aspect of the present invention there is provided a system for generating a two- or three-dimensional image of a radioactivity emitting source in a body, the system comprising (a) a radioactive emission detector; (b) a position tracking system being connected to and/or communicating with the radioactive emission detector; and (c) a data processor being designed and configured for receiving data inputs from the position tracking system and from the radioactive emission detector and for generating the two- or three-dimensional image of the radioactivity emitting source.

According to still another aspect of the present invention there is provided a method of generating a two- or three-dimensional image of a radioactivity emitting source in a body, the system comprising (a) scanning the body with a radioactive emission detector; (b) using a position tracking system

20

being connected to and/or communicating with the radioactive emission detector for determining a position in a two- or three-dimensional system of coordinates of the radioactive emission detector; and (c) data processing inputs from the position tracking system and from the radioactive emission detector for generating the two- or three-dimensional image of the radioactivity emitting source.

According to still another aspect of the present invention there is provided a system for performing an intrabody surgical procedure on a radiopharmaceutical uptaking portion of a body component within a subject, the system comprising a surgical instrument being connected to and/or communicating with a position tracking system for tracking a position of the surgical instrument in a system-of-coordinates, the surgical instrument including a radioactive emission detector coupled thereto for monitoring the radiopharmaceutical in situ. Preferably, radioactive emission detector is sensitive to beta radiation and/or positron radiation. Optionally it is sensitive to low energy (10 – 30 KeV) or gamma radiation. The surgical instrument preferably includes a tissue resecting mechanism and/or a tissue sampling mechanism, such as an aspiration mechanism.

According to an additional aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising (a) a surgical instrument designed and constructed for invading a body of a subject, the surgical instrument including a radioactive emission detector connected thereto or integrated therein; (b) a position tracking system being connected to and/or communicating with the surgical instrument; and (c) a data processor being designed and configured for receiving data inputs from the position tracking system and from the radioactive emission detector and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

According to yet an additional aspect of the present invention there is provided a system for calculating a position of a radioactivity emitting source in

21

a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising (a) a surgical instrument designed and constructed for invading a body of a subject, the surgical instrument including a radioactive emission detector connected thereto or integrated therein; (b) a position tracking system being connected to and/or communicating with the surgical instrument; and (c) a data processor being designed and configured for (i) receiving data inputs from the position tracking system and from the radioactive emission detector; (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; (iii) calculating the position of the surgical instrument in the first system-of-coordinates; and (iii) projecting the position of the radioactivity emitting source and of the surgical instrument onto the second system-of-coordinates.

According to still an additional aspect of the present invention there is provided a method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the method comprising the steps of (a) providing a surgical instrument designed and constructed for invading a body of a subject, the surgical instrument including a radioactive emission detector connected thereto or integrated therein, the surgical instrument being connected to or communicating with a position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the radioactive emission detector in the first system-of-coordinates, thereby defining the positions of the radioactivity emitting source and of the surgical instrument in the first system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

According to a further aspect of the present invention there is provided a system for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject,

22

the system comprising (a) a two- or three-dimensional imaging modality being connected to and/or communicating with a first position tracking system for calculating the position of the body component in a first system-of-coordinates; (b) a surgical instrument designed and constructed for invading the body, the 5 surgical instrument including a radioactive emission detector connected thereto or integrated therein, the surgical instrument being connected to and/or communicating with a second position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and (c) at least one data processor being designed and 10 configured for receiving data inputs from the three-dimensional imaging modality, the first position tracking system, the radioactive emission detector and the second position tracking system and calculating the position of the body component, the position of the radiopharmaceutical uptaking portion of the body component and the position of the surgical instrument in a common 15 system-of-coordinates.

According to yet a further aspect of the present invention there is provided a method for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the method comprising the steps of (a) providing a two- or 20 three-dimensional imaging modality being connected to and/or communicating with a first position tracking system and calculating the position of the body component in a first system-of-coordinates; (b) providing a surgical instrument designed and constructed for invading the body, the surgical instrument including a radioactive emission detector connected thereto or integrated 25 therein, the surgical instrument being connected to and/or communicating with a second position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and (c) receiving data inputs from the two- or three-dimensional imaging modality, the first position tracking system, the 30 radioactive emission detector and the second position tracking system and

23

calculating the position of the body component, the position of the surgical instrument and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

The present invention seeks to improve and expand upon generation of  
5 one, two- or three-dimensional images of radioactivity emitting sources. Specifically, the present invention seeks to provide an improved method and system for imaging and guiding a diagnostic or therapeutic instrument towards a target region inside the patient's body, particularly by means of a nuclear radiation detector with a position tracking system.

10 In one aspect of the invention, a radiation probe is housed in a collimator and attached to a position tracking system. As the probe moves in two- or three-dimensional space about the patient being examined, data is collected and an image of the radiation patterns emanating from within the patient are mapped. One advantage of a two- or three-dimensional scan is that higher safety  
15 and accuracy are achieved through a greater number of directional searches and in turn a better localization of the radiation source.

20 The invention enables mapping radiation source regions and surrounding uncertainty regions. One way of accomplishing this is by means of a feedback system that employs statistical analysis to determine the bounds of an uncertainty region, and which guides medical personnel to conduct additional scans in these uncertainty regions to improve accuracy, reduce error, and hence minimize the bounds of the uncertainty regions.

25 The present invention successfully addresses the shortcomings of the presently known configurations by providing a radioactive emission detector per se and/or integrated in a surgical instrument connected to or communicating with a position tracking system and the use thereof in a variety of systems and methods used for medical imaging and/or medical procedures.

The present invention has many other applications in the direction of therapeutics, such as, but not limited to, implanting brachytherapy seeds,

24

ultrasound microwave radio-frequency cryotherapy and localized radiation ablations.

Implementation of the methods and systems of the present invention involves performing or completing selected tasks or steps manually, 5 automatically, or a combination thereof. Moreover, according to actual instrumentation and equipment of preferred embodiments of the methods and systems of the present invention, several selected steps could be implemented by hardware or by software on any operating system of any firmware or a combination thereof. For example, as hardware, selected steps of the invention 10 could be implemented as a chip a circuit. As software, selected steps of the invention could be implemented as a plurality of software instructions being executed by a computer using any suitable algorithms. In any case, selected steps of the method and system of the invention could be described as being performed by a data processor, such as a computing platform for executing a 15 plurality of instructions.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the 20 drawings in detail, it is stressed that the particulars shown are by way of example and purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is 25 made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

FIG. 1 is a black box diagram of a system according to the teachings of the present invention;

5 FIG. 2 is a perspective view of an articulated arm which serves as a position tracking system shown carrying a radioactive emission detector in accordance with the teachings of the present invention;

10 FIG. 3 is a schematic depiction of a radioactive emission detector carrying a pair of three coaxially aligned accelerometers which serve as a position tracking system in accordance with the teachings of the present invention;

FIG. 4 is a schematic presentation of a radioactive emission detector communicating with yet another type of a position tracking system in accordance with the teachings of the present invention;

15 FIG. 5 is a simplified cross-sectional view of a narrow or wide angle radioactive emission detector used to implement an embodiment of the present invention;

FIG. 6 is a presentation of a scanning protocol which can be effected with the detector of Figure 5;

20 FIG. 7 is a simplified cross-sectional view of a spatially sensitive radioactive emission detector, e.g., a gamma camera, used to implement another embodiment of the present invention;

FIG. 8 is a presentation of a scanning protocol which can be effected with the detector of Figure 7;

25 FIG. 9 demonstrates a system in accordance with the teachings of the present invention which employs four position tracking systems for co-tracking the positions of a patient, a radioactive emission detector, an imaging modality and a surgical instrument;

30 FIG. 10 demonstrates the use of a pair of radiation emission detectors connected therebetween via a connector, preferably a flexible connector or a flexible connection to the connector according to the present invention;

<sup>26</sup>

FIG. 11 is a schematic diagram of a surgical instrument and accompanying system elements according to the teachings of the present invention;

5 FIG. 12 is a simplified pictorial illustration of an imaging system constructed and operative in accordance with a preferred embodiment of the present invention, including a radiation probe and position sensor, position tracking system, medical imaging system and coordinate registration system;

10 FIG. 13 is a simplified pictorial illustration of a single dimension image formation with a nuclear radiation probe attached to a position tracking system of the system of Figure 12, in accordance with a preferred embodiment of the present invention;

FIG. 14 is a simplified pictorial plot of detecting a radiation point source with the nuclear radiation probe of the system of Figure 12, without further processing, in accordance with a preferred embodiment of the present invention;

15 FIG. 15 is a simplified flow chart of an averaging algorithm used in the imaging system of Figure 12, in accordance with a preferred embodiment of the present invention;

20 FIG. 16 is a simplified pictorial plot of detecting a radiation point source with the nuclear radiation probe of the system of Figure 12, with averaging processing, in accordance with a preferred embodiment of the present invention;

FIGS. 17 and 18 are simplified pictorial illustrations of hot cross and hot bar phantom images, respectively, of images produced by a gamma radiation probe of the system of Figure 12;

25 FIG. 19 is a simplified flow chart of a minimizing algorithm used in the imaging system of Figure 12, in accordance with a preferred embodiment of the present invention;

FIG. 20 is a simplified pictorial plot of detecting a radiation point source with the nuclear radiation probe of the system of Figure 12, with minimizing processing, in accordance with a preferred embodiment of the present invention;

27

FIG. 21 is a simplified pictorial illustration of an image reconstruction system constructed and operative in accordance with a preferred embodiment of the present invention, which produces a combined image made up of medical images, the position of the peak radiation location and the location of a therapeutic instrument;

FIG. 22 is a simplified flow chart of a radiation map reconstruction algorithm, in accordance with a preferred embodiment of the present invention;

FIGs. 23A and 23B are illustrations of radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of an autonomous adenoma of a thyroid;

FIGs. 24A and 24B are illustrations of radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of suspected Paget's disease of a humerus;

FIGs. 25A and 25B are illustrations of radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of chronic osteomyelitis; and

FIGs. 26A and 26B are illustrations of radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of skeletal metastasis from medulloblastoma.

FIGs. 27A-G demonstrate the operation of an algorithm provided by the present invention for estimating the distribution of radiation sources in a control volume.

#### DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a radioactive emission detector equipped with a position tracking system which can be functionally integrated with medical two- or three-dimensional imaging modalities and/or with guided minimally-invasive or other surgical tools. The present invention can be used for calculating the position of a concentrated radiopharmaceutical in the body in positional context of imaged portions of the body, which information can be

used, for example, for performing an efficient and highly accurate minimally invasive surgical procedure.

The principles and operation of the present invention may be better understood with reference to the drawings and accompanying descriptions.

5 Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it  
10 10 is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

The use of radioactive materials to tag physiologically active tissue within the body of a patient, for determining the tissue's localization and demarcation by radioactive emission detectors has been disclosed in the medical  
15 literature for at least forty years. Significant developments in the localization and demarcation of tissue bearing radioactive isotope tags for diagnostic and/or therapeutic purposes have occurred since that time. In fact, it is now becoming an established practice in the diagnosis and/or treatment of certain diseases, e.g., cancer, blood clots, myocardial infarct and abscesses, to introduce monoclonal  
20 antibodies or other agents, e.g., fibrinogen, fluorodeoxyglucose labeled with a radioactive isotope (e.g.,  $^{99}\text{M}$ Technetium,  $^{67}\text{Gallium}$ ,  $^{201}\text{Thallium}$ ,  $^{111}\text{Indium}$ ,  $^{123}\text{Iodine}$ ,  $^{18}\text{Fluorine}$  and  $^{125}\text{Iodine}$ ) into the body of the patient. Such radiopharmaceuticals tend to localize in particular tissue or cell type, whereas uptake or binding of the specific radiopharmaceutical is increased in more  
25 "physiologically active" tissue such as the active core of a cancerous tissue, so that the radiation emitted following nuclear disintegrations of the isotope can be detected by a radiation detector to better allocate the active portion of a tumor. Such radiation may be, for example,  $\alpha$ ,  $\beta^-$ ,  $\beta^+$  and/or  $\gamma$  radiation.

29

In another type of applications radioactive substances are used to determine the level of flow of blood in blood vessels and the level of perfusion thereof into a tissue, e.g., coronary flow and myocardial perfusion.

Referring now to the drawings, Figure 1 illustrates a system for calculating a position of a radioactivity emitting source in a system-of-coordinates, in accordance with the teachings of the present invention, which system is referred to hereinbelow as system 20.

System 20 includes a radioactivity emission detector 22. System 20 according to the present invention further includes a position tracking system 24. System 24 is connected to and/or communicating with radioactive emission detector 22 so as to monitor the position of detector 22 in a two- or three-dimensional space defined by a system-of-coordinates 28 in two, three or more, say four, five or preferably six degrees-of-freedom ( $x, y, z, \rho, \theta$  and  $\phi$ ). System 20 further includes a data processor 26. Data processor 26 is designed and configured for receiving data inputs from position tracking system 24 and from radioactive emission detector 22 and, as is further detailed below, for calculating the position of the radioactivity emitting source in system-of-coordinates 28. The phrases "system-of-coordinates" and "three-dimensional space" are used herein interchangeably. As shown in Figure 10, a pair (or more) of detectors 22 connected therebetween via a physical connector, each of detectors 22 is position tracked, can be used for calculating the position of the radioactivity emitting source in system-of-coordinates 28. If more than a single detector 22 is used, detectors 22 are preferably connected there between via a connector 29. Connector 29 is preferably flexible. In the alternative, the connections of detectors 22 to connector 29 provide the required flexibility.

Position tracking systems *per se* are well known in the art and may use any one of a plurality of approaches for the determination of position in a two- or three-dimensional space as is defined by a system-of-coordinates in two,

30

three and up to six degrees-of-freedom. Some position tracking systems employ movable physical connections and appropriate movement monitoring devices (e.g., potentiometers) to keep track of positional changes. Thus, such systems, once zeroed, keep track of position changes to thereby determine actual 5 positions at all times. One example for such a position tracking system is an articulated arm.

Figure 2 shows an articulated arm 30 which includes six arm members 32 and a base 34, which can therefore provide positional data in six degrees-of-freedom. Monitoring positional changes may be effected in any one 10 of several different ways. For example, providing each arm member 32 with, e.g., potentiometers or optical encoders 38 used to monitor the angle between adjacent arm members 32, to thereby monitor the angular change of each such arm member with respect to adjacent arm members, so as to determine the position in space of radioactive emission detector 22, which is physically 15 connected to articulated arm 30.

As is shown in Figure 3 other position tracking systems can be attached directly to radioactive emission detector 22 in order to monitor its position in space. An example of such a position tracking system is an assortment of three triaxially (e.g., co-orthogonally) oriented accelerometers 36 which may be used 20 to monitor the positional changes of radioactive emission detector 22 with respect to a space. A pair of such assortments, as is specifically shown in Figure 3, can be used to determine the position of detector 22 in six-degrees of freedom.

As is shown in Figures 4 and 10, other position tracking systems 25 re-determine a position irrespective of previous positions, to keep track of positional changes. Such systems typically employ an array of receivers/transmitters 40 which are spread in known positions in a three-dimensional space and transmitter(s)/receiver(s) 42, respectively, which are in physical connection with the object whose position being monitored. 30 Time based triangulation and/or phase shift triangulation are used in such cases

31

to periodically determine the position of the monitored object, radioactive emission detector 22 in this case. Examples of such a position tracking systems employed in a variety of contexts using acoustic (e.g., ultrasound) electromagnetic radiation (e.g., infrared, radio frequency) or magnetic field and optical decoding are disclosed in, for example, U.S. Pat. Nos. 5,412,619; 6,083,170; 6,063,022; 5,954,665; 5,840,025; 5,718,241; 5,713,946; 5,694,945; 5,568,809; 5,546,951; 5,480,422 and 5,391,199, which are incorporated by reference as if fully set forth herein.

Radioactive emission detectors are well known in the art and may use 10 any one of a number of approaches for the determination of the amount of radioactive emission emanating from an object or portion thereof. Depending on the type of radiation, such detectors typically include substances which when interacting with radioactive decay emitted particles emit either electrons or photons in a level which is proportional over a wide linear range of operation to 15 the level of radiation impinging thereon. The emission of electrons or photons is measurable and therefore serves to quantitatively determine radiation levels. Solid-state detectors in the form of N-type, P-type, PIN-type pixellated or unpixellated include, for example, Ge, Si, CdTe, CdZnTe, CdSe, CdZnSe, HgI<sub>2</sub>, TlBrI, GaAs, InI, GaSe, Diamond, TlBr, PbI<sub>2</sub>, InP, ZnTe, HgBrI, a-Si, a-Se, BP, 20 GaP, CdS, SiC, AlSb, PbO, BiI<sub>3</sub> and ZnSe detectors. Gas (e.g., CO<sub>2</sub> CH<sub>4</sub>) filled detectors include ionization chamber detectors, proportional chamber detectors and geiger chamber detectors. Scintillation detectors include organic scintillators crystals and liquids, such as C<sub>14</sub>H<sub>10</sub> , C<sub>14</sub>H<sub>12</sub> , C<sub>10</sub>H<sub>8</sub>, etc., Plastics, NE102A, NE104, NE110, Pilot U and inorganic scintillators, such as NaI, CsI, 25 BGO, LSO, YSO, BaF, ZnS, ZnO, CaWO<sub>4</sub> and CdWO<sub>4</sub>. Also known are scintillation fiber detectors. Scintillator coupling include photomultiplier tube (PMT) of the following types: side-on type, head-on type, hemispherical type, position sensitive type, icrochannel plate-photomultiplier (MCP-PMTs) and electron multipliers, or photodiodes (and photodiodes arrays), such as Si

<sup>32</sup>

photodiodes, Si PIN photodiodes, Si APD, GaAs(P) photodiodes, GaP and CCD.

Figure 5 shows a narrow angle or wide angle radioactive emission detector 22'. Narrow or wide angle radioactive emission detector 22' includes a 5 narrow slit (collimator) so as to allow only radiation arriving from a predetermined angular direction (e.g., 1° - 280° - wide angle, preferably 1° - 80° - narrow angle) to enter the detector. Narrow or wide angle radioactive emission detectors especially suitable for the configuration shown in Figure 10 are manufactured, for example, by Neoprobe, Dublin, Ohio 10 (www.neoprobe.com), USA, Nuclear Fields, USA (www.nufi.com) IntraMedical Imaging, Los Angeles, CA, USA (www.gammaprobe.com).

As is shown in Figure 6, such a detector is typically used to measure radioactivity, point by point, by scanning over the surface of a radioactive object from a plurality of directions and distances. In the example shown, scans from 15 four different directions are employed. It will be appreciated that if sufficient radioactivity records are collected from different angles and distances, and the orientation and position in space of detector 22' is simultaneously monitored and recorded during such scans, a three-dimensional model of a radioactive region can be reconstituted and its position in space determined. If two or more 20 detectors are co-employed, as shown in the configuration of Figure 10, the results may be collected faster.

Figure 7 shows another example of a radioactive emission detector, a spatially sensitive (pixelated) radioactive emission detector 22" (such as a gamma camera). Detector 22", in effect, includes an array of multitude narrow 25 angle detector units 23. Such an arrangement is used in accordance with the teachings of the present invention to reduce the amount of measurements and angles necessary to acquire sufficient data so as to reconstitute a three-dimensional model of the radioactive object. Examples of spatially sensitive radioactive emission detectors employed in a variety of contexts are 30 disclosed in, for example, U.S. Pat. Nos. 4,019,057; 4,550,250; 4,831,262; and

<sup>33</sup>

5,521,373; which are incorporated by reference as if set forth herein. An additional example is the COMPTON detector (<http://www.ucl.ac.uk/MedPhys/posters/giulia/giulia.htm>). Figure 8 shows a scan optionally made by spatially sensitive radioactive emission detector 22" (such as a gamma camera).

A radioactive emmission detector of particular advantages for use in context of the present invention is the Compton gamma probe, since, in the Compton gamma probe, spatial resolution is independent of sensitivity and it appears possible to exceed the noise equivalent sensitivity of collimated imaging systems especially for systems with high spatial resolution. The Compton probe is a novel type of gamma-probe that makes use of the kinematics of Compton scattering to construct a source image without the aid of mechanical collimators. Compton imaging telescopes were first built in the 1970s for astronomical observations [V. Schoenfelder et al., Astrophysical Journal 217 (1977) 306]. The first medical imaging laboratory instrument was proposed in the early 1980s [M. Singh, Med. Phys. 10 (1983) 421]. The potential advantages of the Compton gamma probe include higher efficiency, 3-D imaging without detector motion, and more compact and lightweight system. In the Compton gamma probe, high-energy gamma rays are scattered from a first detector layer (or detectors array) into a second detector layer array. For each gamma, the deposited energy is measured in both detectors. Using a line drawn between these two detectors, the Compton scattering equation can be solved to determine the cone of possible direction about this axis on which the gamma ray must have entered the first detector. The intersection of cones from many events is then developed to locate gamma ray sources in the probe's field-of-view. Obviously only coincident events are considered, and the more accurately their energy can be determined, the less uncertainty there is in the spatial angle of the arrival cone. The probe's electronic system is combining coincidence measurements across many detectors and detectors layers with a very good energy resolution. The choice of the geometry and the material of

34

the first layer detector plays a major role in the system imaging capability and depends on (i) material efficiency of single Compton events, in relation to other interactions; (ii) detector energy resolution; and (iii) detector position resolution. In particular, the overall angular resolution results from the  
5 combination of two components, related to the energy resolution and to the pixel volume of the detector.

Thus, as now afforded by the present invention, connecting a radioactive emission detector to a position tracking system, permits simultaneous radioactivity detecting and position tracking at the same time. This enables the  
10 accurate calculation of the shape, size and contour of the radiating object and its precise position in a three-dimensional space.

The present invention thus provides a method for defining a position of a radioactivity emitting source in a system-of-coordinates. The method is effected by (a) providing a radioactive emission detector which is connected to or  
15 communicating with a position tracking system; and (b) monitoring radioactivity emitted from the radioactivity emitting source, while at the same time, monitoring the position of radioactive emission detector in the system-of-coordinates, thereby defining the position of the radioactivity emitting source in the system-of-coordinates.

It will be appreciated by one of skills in the art that the model produced by system 20 is projectable onto any of the other systems-of-coordinates, or alternatively, the system-of-coordinates defined by position tracking system 24 may be shared by other position tracking systems, as is further detailed hereinbelow, such that no such projection is required.  
20

Thus, as is further shown in Figure 1, system 20 of the present invention can be used for calculating a position of a radioactivity emitting source in a first system-of-coordinates 28 and further for projecting the position of the radioactivity emitting source onto a second system-of-coordinates 28'. The system includes radioactive emission detector 22, position tracking system 24  
25 which is connected to and/or communicating with radioactive emission detector  
30

35

22, and data processor 26 which is designed and configured for (i) receiving data inputs from position tracking system 24 and from radioactive emission detector 22; (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; and (iii) projecting the position of the 5 radioactivity emitting source onto the second system-of-coordinates.

A method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates is also offered by the present invention. This method is effected by (a) providing a radioactive 10 emission detector being connected to or communicating with a position tracking system; and (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of the radioactive emission detector in the first system-of-coordinates, thereby defining the position of the radioactivity emitting source in the first 15 system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

It will be appreciated that the combination of a radioactive emission detector and a position tracking system connected thereto and/or communicating therewith allows a suitable data processor to generate a two- or 20 three-dimensional image of the radioactivity emitting source. An algorithm can be used to calculate image intensity based on, for example, a probability function which averages radiation counts and generates an image in which the shorter the time interval between radioactive counts, the brighter the image and *vise versa*, while down-compensating when a location is re-scanned. A 25 free-hand scanning with a directional detector can be employed for this purpose.

In one embodiment, when scanning a body area with the detector, the detector is made to follow a three-dimensional surface which defines the body curvature and in effect is used also as a position tracking pointer. This information can be used to define the position of the radioactive source with 30 respect to the outer surface of the body, so as to create a three-dimensional map

36

of both the radioactive source and of the body curvature. This approach can also be undertaken in open surgeries, such as open chest surgeries so as to provide the surgeon in real time with information concerning the functionality of a tissue.

5       The radioactive emission detector which can be used in context of the present invention can be a beta emission detector, a gamma emission detector, a positron emission detector or any combination thereof. A detector that is sensitive to both beta (and/or positron) and gamma emission can be used to improve localization by sensing for example gamma emission distant from the  
10      source and sensing beta or positrons emission closer to the source. A beta detector is dedicated for the detection of either electrons from sources such as  $^{131}\text{I}$ odine, or positrons from sources such as  $^{18}\text{F}$ luorine. A gamma detector can be designed as a single energy detector or as a detector that can distinguish between different types of energies, using the light intensity in the scintillator as  
15      a relative measure of the gamma energy. Also, the detector can be designed to utilize coincidence detection by using detectors facing one another (180 degrees) with the examined organ or tissue in-between. The radiation detector can have different collimators with different diameters. A large bore will be used for high sensitivity with lower resolution while a small bore collimator will  
20      have higher resolution at the expense of lower sensitivity.

Another possibility is to have a the collimator moving or rotating with the opening eccentric so that a different solid angle is exposed to the incoming photons at any one time, thus gathering the photons from overlapping volumes at different time intervals. The rest of the image processing is similar if the  
25      probe moves or if the collimator eccentric opening moves.

System 20 of the present invention can be used in concert with other medical devices, such as, but not limited to, any one of a variety of imaging modalities and/or surgical instruments.

30      Imaging modalities are well known in the art, the main modalities that serve for two- (projectional or cross sectional) or three- (cosequitive cross

sectional) dimensional imaging are a fluoroscope, a computerized tomography scanner, a magnetic resonance imager an ultrasound imager and an optical camera.

Medical images taken of the human body are typically acquired or  
5 displayed in three main orientations (i) coronal orientation: in a cross section (plane), for example, across the shoulders, dividing the body into front and back halves; (ii) sagittal orientation: in a cross section (plane), for example, down the middle, dividing the body into left and right halves; and (iii) axial orientation: in a cross section (plane), perpendicular to the long axis of the body, dividing the  
10 body into upper and lower halves. Oblique views can also be acquired and displayed.

Various types of X-ray imaging are central to diagnosis of many types of cancer. Conventional X-ray imaging has evolved over the past 100 years, but the basic principal is still the same as in 1895, when first introduced. An X-ray  
15 source is turned on and X-rays are radiated through the body part of interest and onto a film cassette positioned under or behind the body part. The energy and wavelength of the X-rays allows them to pass through the body part and create the image of the internal structures like bones. As the X-rays pass through the hand, for instance, they are attenuated by the different density tissues they  
20 encounter. Bone attenuates a great deal more of the X-rays than the soft tissue surrounding it because of its greater density. It is these differences in absorption and the corresponding varying exposure level of the film that creates the images. In fact, X-ray imaging results in a projection of the integrated density of column-voxels defined by the X-rays as they pass through the body.

Fluoroscopy is a method based on the principals of film X-ray that is useful for detecting disorders and tumors in the upper gastro-intestinal (GI) system (for example, the stomach and intestines). Fluoroscopic imaging yields a moving X-ray picture. The physician can watch the screen and see an image of the patient's body (for example the beating heart). Fluoroscopic technology  
30 improved greatly with the addition of television cameras and fluoroscopic

38

"image intensifiers". Today, many conventional X-ray systems have the ability to switch back and forth between the radiographic and fluoroscopic modes. The latest X-ray systems have the ability to acquire the radiograph or fluoroscopic movie using digital acquisition.

5 Computed Tomography (CT) is based on the X-ray principal, where the film is replaced by a detector that measures the X-ray profile. Inside the covers of the CT scanner is a rotating frame which has an X-ray tube mounted on one side and the detector mounted on the opposite side. A fan beam of X-ray is created as the rotating frame spins the X-ray tube and detector around the patient. Each time the X-ray tube and detector make a 360° rotation, an image or "slice" has been acquired. This "slice" is collimated to a thickness between 1 mm and 10 mm using lead shutters in front of the X-ray tube and X-ray detector.

10

As the X-ray tube and detector make this 360° rotation, the detector takes numerous profiles of the attenuated X-ray beam. Typically, in one 360° lap, 15 about 1,000 profiles are sampled. Each profile is subdivided spatially by the detectors and fed into about 700 individual channels. Each profile is then backwards reconstructed (or "back projected") by a dedicated computer into a two-dimensional image of the "slice" that was scanned.

The CT gantry and table have multiple microprocessors that control the 20 rotation of the gantry, movement of the table (up/down and in/out), tilting of the gantry for angled images, and other functions such as turning the X-ray beam on and off. The CT contains a slip ring that allows electric power to be transferred from a stationary power source onto the continuously rotating gantry. The innovation of the power slip ring has created a renaissance in CT called spiral or 25 helical scanning. These spiral CT scanners can now image entire anatomic regions like the lungs in a quick 20 to 30 second breath hold. Instead of acquiring a stack of individual slices which may be misaligned due to slight patient motion or breathing (and lung/abdomen motion) in between each slice acquisition, spiral CT acquires a volume of data with the patient anatomy all in 30 one position. This volume data set can then be computer-reconstructed to

39

provide three-dimensional models such as of complex blood vessels like the renal arteries or aorta. Spiral CT allows the acquisition of CT data that is perfectly suited for three-dimensional reconstruction.

MR Imaging is superior to CT in detecting soft tissue lesions such as  
5 tumors as it has excellent contrast resolution, meaning it can show subtle soft-tissue changes with exceptional clarity. Thus, MR is often the method of choice for diagnosing tumors and for searching for metastases. MR uses magnetic energy and radio waves to create single or consecutive cross-sectional images or "slices" of the human body. The main component of most MR  
10 systems is a large tube shaped or cylindrical magnet. Also, there are MR systems with a C-shaped magnet or other type of open designs. The strength of the MR systems magnetic field is measured in metric units called "Tesla". Most of the cylindrical magnets have a strength between 0.5 and 1.5 Tesla and most of the open or C-shaped magnets have a magnetic strength between 0.01 and  
15 0.35 Tesla.

Inside the MR system a magnetic field is created. Each total MR examination typically is comprised of a series of 2 to 6 sequences. An "MR sequence" is an acquisition of data that yields a specific image orientation and a specific type of image appearance or "contrast". During the examination, a  
20 radio signal is turned on and off, and subsequently the energy which is absorbed by different atoms in the body is echoed or reflected back out of the body. These echoes are continuously measured by "gradient coils" that are switched on and off to measure the MR signal reflecting back. In the rotating frame of reference, the net magnetization vector rotates from a longitudinal position a  
25 distance proportional to the time length of the radio frequency pulse. After a certain length of time, the net magnetization vector rotates 90 degrees and lies in the transverse or x-y plane. It is in this position that the net magnetization can be detected on MRI. The angle that the net magnetization vector rotates is commonly called the 'flip' or 'tip' angle. At angles greater than or less than 90  
30 degrees there will still be a small component of the magnetization that will be in

40

the x-y plane, and therefore be detected. Radio frequency coils are the "antenna" of the MRI system that broadcasts the RF signal to the patient and/or receives the return signal. RF coils can be receive-only, in which case the body coil is used as a transmitter; or transmit and receive (transceiver). Surface coils 5 are the simplest design of coil. They are simply a loop of wire, either circular or rectangular, that is placed over the region of interest.

A digital computer reconstructs these echoes into images of the body. A benefit of MRI is that it can easily acquire direct views of the body in almost any orientation, while CT scanners typically acquire cross-sectional images 10 perpendicular or nearly perpendicular to the long body axis.

Ultrasound imaging is a versatile scanning technique that uses sound waves to create images of organs or anatomical structures in order to make a diagnosis. The ultrasound process involves placing a small device called a transducer, against the skin of the patient near the region of interest, for 15 example, against the back to image the kidneys. The ultrasound transducer combines functions of emitting and receiving sound. This transducer produces a stream of inaudible, high frequency sound waves which penetrate into the body and echo off the organs inside. The transducer detects sound waves as they echo back from the internal structures and contours of the organs. 20 Different tissues reflect these sound waves differently, causing a signature which can be measured and transformed into an image. These waves are received by the ultrasound machine and turned into live pictures with the use of computers and reconstruction software.

Ultrasound scanning has many uses, including: diagnosis of disease and 25 structural abnormalities, helping to conduct other diagnostic procedures, such as needle biopsies etc.

There are limitations to some ultrasound techniques: good images may not be obtained in every case, and the scan may not produce as precise results as some other diagnostic imaging procedures. In addition, scan results may be

41

affected by physical abnormalities, chronic disease, excessive movement, or incorrect transducer placement.

Both two- (cross sectional) and three- (consecutive cross-sectional) ultrasound imaging techniques are available nowadays. Worth mentioning is  
5 the Doppler three-dimensional ultrasound imaging.

In many cases imaging modalities either inherently include (e.g., fluoroscope, CT, MRI) and/or are integrated with position-tracking-systems, which enable the use of such systems to reconstruct three-dimensional image models and provide their position in a three-dimensional space.

10 It will be appreciated that, similar to the vision system, also an optical camera can be used to generate three-dimensional imagery date according to the present invention by imaging a body from a plurality (at least two) directions. This type of imaging is especially applicable in open chest surgeries or other open surgeries. Software for calculating a three-dimensional image from a pair  
15 of stereoscopic images is well known in the art.

Thus, as used herein and in the claims section that follows, the phrase "three-dimensional imaging modality" refers to any type of imaging equipment which includes software and hardware for generating a three-dimensional image. Such an equipment can generate a three-dimensional image by imaging  
20 successive cross-sections of a body, e.g., as if viewed from a single direction. Alternatively, such an equipment can generate a three-dimensional image by imaging a body from different angles or directions (typically two angles) and thereafter combining the data into a three-dimensional image.

Surgical instruments are also well known in the art and may use any one  
25 of a plurality of configurations in order to perform minimally-invasive surgical procedures. Examples include laser probes, cardiac and angioplasty catheters, endoscopic probes, biopsy needles, aspiration tubes or needles, resecting devices, ultrasonic probes, fiber optic scopes, laparoscopy probes, thermal probes and suction/irrigation probes. Examples of such surgical instruments  
30 employed in a variety of medical contexts are disclosed in, for example, U.S.

42

Pat. Nos. 6,083,170; 6,063,022; 5,954,665; 5,840,025; 5,718,241; 5,713,946; 5,694,945; 5,568,809; 5,546,951; 5,480,422 5,391,199, 5,800,414; 5,843,017; 6,086,554; 5,766,234; 5,868,739; 5,911,719; 5,993,408; 6,007,497; 6,021,341; 6,066,151; 6,071,281; 6,083,166 and 5,746,738, which are incorporated by reference as if fully set forth herein.

For some applications, examples of which are provided in the list of patents above, surgical instruments are integrated with position-tracking-systems, which enable to monitor the position of such instruments while placed in and guided through the body of a treated patient.

According to a preferred embodiment of the present invention, the surgical instrument is equipped with an additional radioactive emission detector attached thereto or placed therein. This additional detector is used, according to preferred embodiments of the invention, to fine tune the location of radioactive emission from within the body, and in closer proximity to the radioactive source. Since the surgical tool is preferably connected to or communicating with a position-tracking system, the position of the additional detector can be monitored and its readouts used to fine tune the position of the radioactive source within the body. Thus, according to this aspect of the present invention, at least one extracorporeal detector and an intracorporeal detector are used in concert to determine the position of a radioactive source in the body in highest precision. The extracorporeal detector provides the general position of the source and is used for directing the surgical instrument thereto, whereas the intracorporeal detector is used for reassuring prior to application of treatment or retrieval of biopsy that indeed the source was correctly targeted at the highest precision.

While according to a presently preferred embodiment of the invention two detectors, one extracorporeal and one intracorporeal, are employed as described above, for some applications a single intracorporeal detector may be employed, which detector is attached to or integrated with a surgical instrument whose position is tracked.

43

The use of intracorporeal and extracorporeal detectors calls for careful choice of the radioactive isotope employed with the radiopharmaceutical. While the extracorporeal detector can be constructed with a suitable collimator for handling strong radiation, such as gamma radiation, the intracorporeal detector 5 is miniature by nature and is limited in design and construction by the construction of the surgical instrument with which it is employed. Since collimators for high energy (80 – 511 KeV) gamma radiation are robust in nature, they are not readily engageable with miniature detectors. Electron (beta) and positron radiation are characterized by: (i) they highly absorbed by 10 biological tissue as they are of lower energy and higher chemical reactivity; and (ii) they are readily collimated and focused by thin metal collimators. It is also possible to use low energy gamma radiation (10 – 30 KeV) for intracorporal applications since the collimation of these gamma photons can be achieved with thin layers of Tantalum or Tungsten. As such, the radio pharmaceutical of 15 choice is selected to emit both gamma and beta and/or positron radiation, whereas the extracorporeal detector is set to detect the high energy gamma radiation, whereas the intracorporeal detector is set to detect the low energy gamma, beta and/or positron radiation. Isotopes that emit both high energy gamma and/or low energy gamma, beta and/or positron radiation and which can 20 be used *per se* or as a part of a compound as radiopharmaceuticals include, without limitation, <sup>18</sup>F, <sup>111</sup>In and <sup>123</sup>I in radiopharmaceuticals, such as, but not limited to, 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose (<sup>18</sup>FDG), <sup>111</sup>In-Pentetreotide ([<sup>111</sup>In-DTPA-D-Phe<sup>1</sup>]-octreotide), L-3-[<sup>123</sup>I]-Iodo-alpha-methyl-tyrosine (IMT), O-(2-[<sup>18</sup>F]fluoroethyl)-L-tyrosine (L-[<sup>18</sup>F]FET), <sup>111</sup>In-Capromab Pendetide 25 (CYT-356, Prostascint) and <sup>111</sup>In-Satumomab Pendetide (Oncoscint).

Figure 11 illustrates a system in accordance with this aspect of the present invention. A surgical instrument 100 is shown connected to a resection/aspiration control element 102 as well known in the art. Surgical instrument 100 includes a radioactive emission detector 104, which has a 30 collimator 106 for collimating low energy gamma, beta and/or positron

44

radiation. In some embodiments, as indicated by arrow 108, detector 104 may be translated within instrument 100. A position tracking system having one element thereof 110 attached to instrument 100 and another element thereof 112 at a fixed location serves to monitor the position of instrument 100 at all times 5 in two, three and up to six degrees of freedom. Radioactive emission detector 104 communicates with a counter 114 for counting low energy gamma, beta and/or positron radiation. All the data is communicated to, and processed by, a processor 116. The 2D or 3D data may be projected and displayed along with 10 2D or 3D imaging data derived from an imaging modality using a shared presentation device as described elsewhere herein. A real or virtual image of the surgical instrument itself may also be co-displayed. Examples of 15 commercially available radiation emission detectors that can fit inside, for example, a biopsy needle include scintillating plastic optical fibers like S101 and S104, manufactured by PPLASTIFO or an optical fiber communicating with a scintillator (either detector paint or scintillation crystal) at the fiber edge. The level of detected radiation can be reported visually or by an audio signal, as 20 is well known in the art.

Thus, a surgical instrument equipped with a radiation emission detector and which is connected to and/or communicating with a position tracking 25 system forms one embodiment of this aspect of the present invention. Such a design acting in concert with either conventional imaging modalities and/or extracorporeal radiation emission detectors form other embodiments of this aspect of the invention. In all cases, a surgical instrument equipped with a radiation emission detector and which is connected to and/or communicating 30 with a position tracking system serves for *in situ* fine tuning of a radioactive source in the body.

It will be appreciated that in some minimally-invasive procedures even the position of the patient him or herself is monitored via a position tracking system, using, for example, electronic or physical fiducial markers attached at 30 certain locations to the patient's body.

45

Thus, as is further detailed hereinbelow, by projecting the three-dimensional data and positions received from any of the above mentioned devices into a common system of coordinates, or alternatively, employing a common position tracking system for all of these devices, one can integrate the  
5 data into a far superior and comprehensive presentation.

An example to this desired outcome is shown in Figure 9. In the embodiment shown, four independent position tracking systems 50, 52, 54 and 56 are used to track the positions of a patient 58, an imaging modality 60, a radioactive emission detector 62 and a surgical instrument 64 in four  
10 independent systems-of-coordinates 66, 68, 70 and 72, respectively. If the patient is still, no tracking of the patient's position is required.

It will be appreciated that any subset or all of the position tracking systems employed may be integrated into one or more common position tracking systems, and/or that any subset or all of the position tracking systems  
15 employed may share one or more systems-of-coordinates, and further that any positional data obtained by any of the position tracking systems described in any of the systems-of coordinates may be projected to any other system of coordinates or to an independent (fifth) system of coordinates 74. In one preferred embodiment, applicable for applications at the torso of the patient, the  
20 system of coordinates is a dynamic system of coordinates which takes into account the chest breathing movements of the patient during the procedure.

As indicated at 76, the raw data collected by detector 62 is recorded and, as indicated at 78, the position and the radioactive data records are used to generate a three-dimensional model of a radiopharmaceutical uptaking portion  
25 of a body component of the patient.

Similarly, as indicated at 80, the imagery data collected by imaging modality 60 is recorded and the position and the imagery data records are used to generate a three-dimensional model of the imaged body component of the patient.

46

All the data collected is then fed into a data processor 82 which processes the data and, as indicated at 84, generates a combined or superimposed presentation of the radioactive data and the imagery data, which is in positional context with patient 58 and surgical instrument 64.

5       Instrument 64, which by itself can be presented in context of the combined presentation, may then be used to perform the procedure most accurately. Processor 82 may be a single entity or may include a plurality of data processing stations which directly communicate with, or even integral to, any one or more of the devices described.

10      The present invention provides a major advantage over prior art designs because it positionally integrates data pertaining to a body portion as retrieved by two independent imaging techniques, conventional imaging and radioactive imaging, to thereby provide a surgeon with the ability the fine point the portion of the body to be sampled or treated.

15      It will be appreciated that subsets of the devices described in Figure 9 may be used as stand-alone systems. For example, a combination of detector 62 with its position-tracking system and instrument 64 with its position-tracking-system may in some instances be sufficient to perform intrabody procedures. For mere diagnostic purposes, without biopsy, a  
20 combination of detector 62 position-tracking-system and modality 60 position-tracking-system are sufficient.

Reference is now made to Figure 12, which illustrates an imaging system 200 constructed and operative in accordance with a preferred embodiment of the present invention. Imaging system 200 preferably includes a radiation probe  
25 202, such as the narrow angle radioactive emission detector 22' described hereinabove with reference to Figures 5 and 10.

A position sensor 204 is provided for sensing the position of radiation probe 202. Position sensor 204 may be physically attached to radiation probe 202, or may be distanced therefrom. Position sensor 204 transmits the sensed

47

position data to a position tracking system 206. Position tracking system 206 may be a system like position tracking system 24, described hereinabove with reference to Figure 1, and position sensor 204 may be any kind of sensor applicable for such position tracking systems.

5 Another method which can be used to locate the source of radiation emission is by using a small hand held gamma camera 205 (such as the DigiRad 2020tc Imager TM, 9350 Trade Place, San Diego, California 92126-6334, USA), attached to position sensor 204.

Position tracking system 206 enables radiation probe 202 to freely scan  
10 back and forth in two- or three-dimensions over the area of interest of the patient, preferably incrementing a short distance between each scan pass. Position tracking system 206 tracks the position of radiation probe 202 with respect to a position tracking coordinate system, such as  $X_p$ ,  $Y_p$  and  $Z_p$ , with an origin  $O_p$ .

15 Imaging system 200 also includes a medical imaging system 208, such as, but not limited to, computed or computerized tomography (CT), magnetic resonance imaging (MRI), ultrasound imaging, positron emission tomography (PET) and single photon emission computed tomography (SPECT), for example. Medical imaging system 208 provides images of a patient 209 with  
20 respect to a medical imaging coordinate system, such as  $X_m$ ,  $Y_m$  and  $Z_m$ , with an origin  $O_m$ .

Imaging system 200 also includes a coordinate registration system 210, such as that described in U.S. Patent Application No. 09/610,490, the disclosure of which is incorporated herein by reference. Coordinate registration system  
25 210 is adapted to register the coordinates of the position tracking coordinate system with those of the medical imaging coordinate system.

Position tracking system 206, medical imaging system 208 and coordinate registration system 210 are preferably in wired or wireless

communication with a processing unit 212 (also referred to as a data processor 212).

In operation of imaging system 200, after administration of a radiopharmaceutical to patient 209, a clinician/physician/surgeon (not shown) 5 may move or scan radiation probe 202 about a target area under examination. A physiological activity map of the target area is obtained by measuring the radiation count rate with radiation probe 202, and by correlating the count rate with the count rate direction with position tracking system 206, which follows the motion of the moving or scanning radiation probe 202.

10 Reference is now made to Figure 13 which illustrates image formation with radiation probe 202, in accordance with a preferred embodiment of the present invention. For the purposes of simplicity, the example shown in Figure 13 is for a single dimension image formation, but it is readily understood that the same principles hold true for any other dimensional image formation.

15 In one example of carrying out the invention, radiation probe 202 may be a gamma ray detector probe that comprises a collimator 211 and radiation detector 213. Gamma rays are projected through the probe collimator 211 onto radiation detector 213, which produces electronic signals in accordance with the radiation detected. Radiation probe 202 sends pulses to a probe counter 215 20 which may include a pulse height analyzer circuit (not shown). The pulse height analyzer circuit analyzes the electronic signals produced by radiation detector 213. If the electronic signals are within a selected energy window, the level of radiation, i.e., number of radiation counts, is counted by probe counter 215.

Examples of suitable radiation detectors include a solid state detector 25 (SSD) (CdZnTe, CdTe, HgI, Si, Ge, and the like), a scintillation detector (NaI(Tl), LSO, GSO, CsI, CaF, and the like), a gas detector, or a scintillating fiber detector (S101, S104, and the like), for example.

The position sensor 204 associated with the radiation probe 202 senses the position of radiation probe 202, and position tracking system 206 calculates

49

and monitors the motion of radiation probe 202 with respect to the position tracking coordinate system. The motion is calculated and monitored in two, three and up to six dimensions - the linear directions of the X, Y and Z axes as well as rotations about the X, Y and Z axes (i.e., rotational angles  $\rho$ ,  $\theta$  and  $\varphi$ , respectively).

Examples of suitable position tracking systems include a measurement mechanical arm (FaroArm, <http://www.faro.com/products/faroarm.asp>), optical tracking systems (Northern Digital Inc., Ontario, Canada NDI-POLARIS passive or active systems), magnetic tracking systems (NDI-AURORA), infrared tracking systems (E-PEN system, <http://www.e-pen.com>), and ultrasonic tracking systems (E-PEN system), for example.

Processing unit 212 combines the radiation probe count rate from probe counter 215 together with the positional information from position tracking system 206, and uses an imaging software algorithm 217 to form a two-dimensional or three-dimensional radiotracer-spread image of the target area inside the patient's body. The spatial probe positions together with the spatial count rates may be stored in memory or displayed on a computer monitor 214 as a pattern of marks corresponding to the spatial and count rate position.

An example of such a pattern is shown in Figure 14, which illustrates a single-dimensional, unprocessed simulation of a radiation point source 218 (Figure 13), 30 mm deep inside the human body, detected by using a 10 mm nuclear radiation probe 202 coupled to position tracking system 206. The graph of Figure 14 indicates to a physician that there is a peak count rate of about 500 in the probe position of about 50 mm.

In one embodiment of the invention, the imaging software algorithm 217 employs an averaging process to refine the curve of Figure 14. This averaging process will now be described with reference to Figure 15.

Probe counter 215 feeds probe count rate information  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  to processing unit 212 (step 301). Position sensor 204 feeds probe position

50

information ( $X_c$ ,  $Y_c$ ,  $Z_c$ ,  $\rho$ ,  $\theta$ ,  $\varphi$ ) to processing unit 212 (step 302). Probe parameters (such as its physical size,  $dx$ ,  $dy$ ,  $dz$ ) are also input into processing unit 212 (step 303).

Processing unit 212 then finds all the voxels (i.e., volume pixels) that represent the probe volume in the processing unit memory (step 304), i.e.,  $X_c+dx$ ,  $Y_c+dy$ ,  $Z_c+dz$ . Processing unit 212 calculates the number of times that the calculation process has been done in each voxel from the beginning of the image formation (step 305), i.e.,  $M(X_c+dx, Y_c+dy, Z_c+dz)$ . Processing unit 212 then calculates the new average count rate values in each voxel (step 306), in accordance with the formula:

$$N(X_c+dx, Y_c+dy, Z_c+dz) = \\ [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / \\ [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$$

Processing unit 212 then corrects the display image that represents the perceived voxels at  $N(X_c+dx, Y_c+dy, Z_c+dz)$  (step 307). The algorithm then repeats itself for the next probe position (step 308).

The resulting graph of the averaging algorithm of Figure 15, as applied to the example of Figure 14, is shown in Figure 16.

Figures 17 and 18 respectively show examples of a hot cross phantom image and a hot 4.77 mm bar phantom image, produced by a gamma radiation probe coupled with position tracking system 206 and the averaging algorithm of Figure 15. The probe images were made by using a probe, EG&G Ortec NaI(Tl) model 905-1 (thickness=1", diameter =1") connected to a ScintiPack model 296. The position tracking system used was the Ascension miniBIRD, commercially available from Ascension Technology Corporation, P.O. Box 527, Burlington, Vermont 05402 USA (<http://www.ascension-tech.com/graphic.htm>). The magnetic tracking and location systems of Ascension Technology Corporation use DC magnetic fields

51

to overcome blocking and distortion from nearby conductive metals. Signals pass through the human body without attenuation.

In another embodiment of the invention, the imaging software algorithm 217 may employ a minimizing process to refine the curve of Figure 14 as is now 5 described with reference to Figure 19.

Probe counter 215 feeds probe count rate information  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  to processing unit 212 (step 401). Position sensor 204 feeds probe position information  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  to processing unit 212 (step 402). Probe parameters (such as its physical size,  $dx, dy, dz$ ) are also input into processing 10 unit 212 (step 403).

Processing unit 212 then finds all the voxels that represent the probe volume in the processing unit memory (step 404), i.e.,  $X_c+dx, Y_c+dy, Z_c+dz$ . From the voxels that represent the probe volume in the processing unit memory, processing unit 212 finds those that have a higher count rate value  $N(X_c+dx, Y_c+dy, Z_c+dz)$  than the inputted probe count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  (step 15 405). Processing unit 212 then changes the higher count rate voxels to that of inputted probe count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  (step 406), and corrects the display image at the higher count rate voxels  $N(X_c+dx, Y_c+dy, Z_c+dz)$  (step 407). The algorithm then repeats itself for the next probe position (step 408).

20 The resulting graph of the minimizing algorithm of Figure 19, as applied to the example of Figure 14, is shown in Figure 20.

Another algorithm is provided by the invention for estimating the distribution of radiation sources in a control volume, and is described with reference to Figures 27A-27G. In this algorithm, it is assumed that the radiation 25 sources comprise dot sources that radiate uniformly in all directions, and that the radiation sources are localized and smoothly distributed in a bounded volume.

Reference is now made to Figures 27A and 27B, which illustrate a radiation sensor 600, preferably generally shaped as a tube collimator. Radiation quanta 602 are registered by the radiation sensor 600, as described hereinabove,

52

thereby providing the average number of quanta per unit time. The radiation sensor 600 may be moved around a volume of interest 604. The position of the sensor 600 and its direction (as well as the position of the investigated volume 604) are assumed to be known at any given moment (Figure 27A).

5 The tube collimator is preferably provided with a plane circular detector 606 of radiation quanta. The quanta detector 606 is preferably disposed on a rear end 608 of the tube and radiation quanta can reach the detector 606 only through an open front end 610 of the tube (Figure 27B)

Reference is now made to Figure 27C, which illustrates a system of  
10 coordinates  $(x, y, z)$  with the origin  $O$  in the center of the radiation sensor 600, the  $(x, y)$  plane being the plane of the detector, and the  $z$  axis being in the center of the collimator tube. The geometry parameters of the collimator tube – height  $h$  and radius  $\rho$  – are known.

From the rotational symmetry of the tube, it is clear that having a  
15 radiation source  $Q = Q(x, y, z)$  with the total intensity  $I$  uniformly radiating in all directions, the portion of the intensity registered by the quanta detector 606 of the radiation sensor 600 is determined only by the distance  $r$  from  $Q$  to the axis of the collimator (axis  $z$ ) and the distance  $z$  from  $Q$  to the  $(x, y)$  plane. In other words, there is a function  $\Phi(r, z)$ , which is defined only by the collimator  
20 parameters  $\rho$  and  $h$  (corresponding expressions from  $\rho$ ,  $h$ ,  $r$  and  $z$  may be easily written in explicit form), such that the intensity of the radiation spot  $Q = Q(x, y, z) = Q(r, z)$  registered by detector 606 is proportional to  $\Phi(r, z)$  and to the total intensity  $I$  of the radiation spot.

Reference is now made to Figure 27D. It follows from the foregoing  
25 discussion, that if instead of one radiation spot there is some radiation distribution  $I(Q) = I(Q(r, z))$  in a volume  $V$ , then the radiation intensity, registered by radiation sensor 600, is proportional (with some constant not depending on the radiation distribution and the sensor position) to the following integral:

$$\int_V I(Q(r, z)) \Phi(r, z) dQ \quad (1)$$

An algorithm for estimating the intensity distribution  $I(Q)$  from the values obtained in the measurement scheme of Equation (1) is now discussed. For the sake of simplicity, the first case is discussed with reference to Figure 5 27E for a two-dimensional problem, wherein intensities  $I(Q)$  are distributed in some 2-dimensional plane. The 3D problem is a direct generalization of the corresponding 2D problem, as is explained hereinbelow.

As seen in Figure 27E, the radiation sources are distributed in a rectangular region  $V$  in a plane. Two systems of coordinates are considered. The 10 first one is the sensor coordinate system  $(x, y, z)$  corresponding to the sensor 600. The second one is the radiation source coordinate system  $(u, v, w)$  corresponding to the radiation sources plane  $(u, v)$ .

It is assumed that at each discrete time increment, the position of the 15 origin of  $(x, y, z)$  system and the direction of the  $z$ -axis unit vector in  $(u, v, w)$  coordinates are known. In other words, the position and direction of the moving sensor in the  $(u, v, w)$  coordinate system is known, and the  $(u, v, w)$  coordinate system is assumed to be motionless.

The radiation sources are considered to be distributed in accordance with the distribution function  $I(Q)$  in some bounded, given rectangle  $V$  on the plane 20  $(u, v)$ .  $I(Q) = I(u, v)$  is the unknown and sought-for radiation (or radiation intensity) distribution function defined in  $V$ .

To regularize the problem of estimation of the radiation distribution function  $I(Q)$ , the function  $I(Q)$  will be considered to be given from some finite dimensional space  $H$  of functions defined in  $V$ . In other words, the function 25  $I(Q)$  itself will not be estimated but rather some finite dimensional approximation of the distribution  $I(Q)$ .

The simplest approach to finite dimensional approximation is to subdivide the rectangle  $V$  into sets of equal rectangular cells and consider the

54

space  $H$  of step-functions corresponding to this subdivision (i.e., the space of functions that are constant in the cells of subdivision), as shown in Figure 27F.

If the subdivision of rectangle  $V$  into small rectangles is sufficiently fine, then this step-function approximation is good enough for the estimation of radiation distribution  $I(Q)$ .

Let each side of rectangle  $V$  be divided into  $n$  equal parts (Figure 27F). Then  $m = n^2$  is the dimension of the space  $H$  of step-functions on the corresponding subdivision.

The space  $H$  is naturally isomorphic to the  $m$ -dimensional space of  $n \times n$  matrixes (with its natural scalar product  $\langle \bullet, \bullet \rangle$ ).

Let  $I = (I_{ij})_{i,j=1,\dots,n}$  be the unknown element of  $H$  that it is desired to estimate. Suppose that element  $I$  is measured on  $K$  functionals  $\{\Phi_k\}_{k=1..K}$  of the form of the integral (1):

$$15 \quad \langle I, \Phi_k \rangle = \sum_{i,j=1..n} I_{ij} \Phi_{ij}^{(k)} \quad (2)$$

where  $\Phi_k = (\Phi_{ij}^{(k)})_{i,j=1,\dots,n}$ ,  $k = 1, \dots, K$  (after approximation of function  $I(Q)$  by the corresponding step-function, the integral (1) is transformed to the sum (2)).

20 Functionals  $\Phi_k$ ,  $k = 1, \dots, K$ , correspond to  $K$  discrete positions of the sensor (Figure 27E). Knowing the explicit expressions for functions  $\Phi(r, z)$  from (1) and knowing for each time moment  $k$ , the position of the sensor relative to inspection region  $V$ , one can calculate all matrixes  $\Phi_k = (\Phi_{ij}^{(k)})_{i,j=1,\dots,n}$ ,  $k = 1, \dots, K$ .

25 Accordingly the following scheme of measurements are obtained:

$$\psi_k = \langle I, \Phi_k \rangle + \varepsilon_k, \quad k = 1, \dots, K. \quad (3)$$

Here  $\psi_k$  are results of measurements of the unknown element  $I$  of the space  $H$ , and  $\varepsilon_k$  are random errors ( $\varepsilon_k$  - independent random variables,  $E\varepsilon_k = 0$ ,  $k = 1, \dots, K$ ).

55

Let  $M: H \rightarrow H$  the operator in the space  $H$  of the form:

$$M = \sum_{k=1..K} \Phi_k \otimes \Phi_k. \quad (4)$$

Then the best non-biased linear estimate  $\hat{I}$  of the element  $I$  is given by the formula:

$$5 \quad \hat{I} = M^{-1} \Psi, \quad (5)$$

where  $M^{-1}: H \rightarrow H$  the inverse operator to the operator  $M$  of the form (4), and

$$\Psi = \sum_{k=1..K} \psi_k \Phi_k, \quad (6)$$

(where  $\psi_k$  are the results of measurements of the form (3)).

10 One problem of using estimates (5) (besides computational problems if the dimension  $m$  of the space  $H$  is very large) is that the operator  $M: H \rightarrow H$  of the form (3) is "bad invertible". In other words, the estimation problem is "ill-posed". It means that having a noise  $\varepsilon_k$  in the measurements scheme (3), even if the noise is small, may sometimes result in a very large estimation error  
15  $\text{dist}(I, \hat{I})$ .

This means that the estimation problem requires additional regularization. This is a general problem of solving a large set of linear equations. There are several methods for solving such equations. Below is described one of the known methods for solving such equations but numerous  
20 other methods are also possible, these include gradient decent methods such as in (<http://www-visl.technion.ac.il/1999/99-03/www/>) and other methods that are generally known in the art. Further, it is possible to improve the image reconstruction by taking into account the correlation between measurements as they are done with substantial overlap. Also, in the following description, a  
25 regular step function is assumed for the representation of the pixels or voxels, other basis may be used such as wavelet basis, gaussian basis, etc., which may be better suited for some applications.

To obtain regularized estimate  $\hat{I}_R$  instead of the estimate  $\hat{I}$ , the eigenvector decomposition of the operator  $M$  may be used:

56

Let  $\varphi_1, \varphi_2, \dots, \varphi_m$  be eigenvectors of operator  $M: H \rightarrow H$  corresponding to eigenvalues  $\lambda_1 \geq \lambda_2 \geq \dots \geq \lambda_m \geq 0$ .

Let  $R$  be some natural number,  $1 < R < m$  ( $R$  is the “regularization parameter”). Let  $H^{(R)}$  be the subspace of the space  $H$  spanned by the first  $R$  eigenvectors  $\varphi_1, \dots, \varphi_R$ .

$$H^{(R)} = \text{sp} \{ \varphi_k \}_{k=1 \dots R}. \quad (7)$$

Let  $P^{(R)}: H \rightarrow H^{(R)}$  be the orthogonal projection on subspace  $H^{(R)}$ .

The regularized estimate  $\hat{I}_R$  may be obtained as follows:

Let  $\Phi_k^{(R)} = P^{(R)} \varphi_k$ ,  $k = 1, \dots, K$ .

$$10 \quad \Psi^{(R)} = \sum_{k=1 \dots K} \psi_k \Phi_k^{(R)}, \quad (8)$$

$M^{(R)}: H^{(R)} \rightarrow H^{(R)}$  the operator of the form:

$$M^{(R)} = \sum_{k=1 \dots K} \Phi_k^{(R)} \otimes \Phi_k^{(R)} \quad (9)$$

(operator  $M^{(R)}$  is the restriction of the operator  $M$  of the form (4) to the subspace  $H^{(R)}$  of the form (7)),

$$15 \quad \text{then } \hat{I}^{(R)} = (M^{(R)})^{-1} \Psi^{(R)}. \quad (10)$$

When the regularization parameter  $R$  is properly chosen (so that the eigenvalue  $\lambda_R$  is not too small), then the estimate (10) becomes stable.

There are several possible approaches to choosing the parameter  $R$ . One approach is to leave  $R$  as a “program parameter” and to obtain the reasonable value “in experiment”. Another approach is to choose some “optimal” value. This is possible if the covariation operators of the random noise  $\varepsilon_k$  in (3) are known, and information about the element  $I$  of the space  $H$  is known *a priori*.

The subdivision into a large number of *equal* rectangles has the disadvantage of making the dimension of the space  $H$  too big (especially in the 3D case). If each side of rectangle  $V$  is subdivided into  $n$  *equal* parts, then the dimension of the space  $H$  will be  $n^2$  and the dimension of the matrices used in solving the corresponding estimation equations would be  $n^2 \times n^2 = n^4$  (in the 3D case,  $n^3 \times n^3 = n^6$ ). It is clear that for large  $n$ , this situation may cause serious memory and computation time.

57

In accordance with a preferred embodiment of the present invention, an irregular subdivision of the rectangle V is used. This irregular approach may significantly decrease the dimension of the problem and facilitate computer calculations.

5 More specifically, a drawback of the regular subdivision of the investigated region V, discussed hereinabove, is that a lot of cells that actually have no signal may be taken into account (Figure 27F). It would be much better to have small cells only in regions with high signal and have big cells in regions with low signal.

10 Reference is now made to Figure 27G, which illustrates an advantageous irregular cell subdivision, in accordance with a preferred embodiment of the present invention.

15 In a first stage, regular subdivisions are made in "large" cells, and measurements and estimations are made as described hereinabove. In this manner, the intensity distribution is estimated in the large cells.

In a second stage, the large cells, which have an intensity larger than some threshold, are subdivided into 4 equal subcells (or 8 subcells in the 3D case). A suitable threshold may be obtained by taking the average intensity (of all large cells) minus two (or three) sigmas (standard deviation), for example.  
20 Measurements and estimations are made in these subdivisions as described hereinabove.

25 The act of subdivision and subsequent measurements and estimations are continued until a desired accuracy is reached at some smaller level of subdivision, typically defined by the computational and memory capabilities of the computer being used.

The 3D problem may be treated in the same way as the 2D case, the only difference being that instead of rectangle V, there is a parallelepiped V (Figure 27D). Accordingly, the cells in each subdivision are also parallelepipeds.

30 The algorithms described hereinabove may be used for a variety of imaging systems. For example, the algorithms may be used with single

radiation detector probe, an array of radiation detector probes, large gamma cameras of various design, such as multi head cameras, general purpose cameras, and automatic white balance (AWB) scanners. The algorithms are suitable for SPECT and planar imaging, and may be used for all types of isotopes of with any type of photon energy.

From the foregoing discussion, the skilled artisan will appreciate that the algorithms described hereinabove may be used to predict the location of the radiation source and the uncertainty region (based on the system measurement errors) in the vicinity of the radiation source. The algorithms also guide the user 10 to perform additional measurements to minimize the uncertainty region according to the requirements of the system operator.

The algorithms thus comprise a feedback system that employs analysis to determine the bounds of an uncertainty region about the radiation source, and which guides medical personnel to conduct additional scans in these uncertainty 15 regions to improve accuracy, reduce error, and hence minimize the bounds of the uncertainty regions.

Continuous sampling with radiation probe 202 may provide localization of a tumor and a physiological radiation activity map of the tumor region. Higher safety and accuracy are gained by a greater number of scans.

Reference is now made to Figure 21 which illustrates an image reconstruction system 450, constructed and operative in accordance with a preferred embodiment of the present invention. Image reconstruction system 450 produces a combined image 451 made up of the images coming from the medical imaging system 208 with the position of the peak radiation location 20 25 (and its uncertainty area) from processing unit 212, together with the location of a therapeutic instrument 452, such as a biopsy needle. The combined image 451 allows the physician to better assess the relative position of therapeutic instrument 452 in relation to the anatomical image (from medical imaging system 208) and the position of the radioactive area as inferred by the radiation detection algorithm.

Reference is now made to Figure 22 which illustrates a flow chart of a radiation map reconstruction algorithm, in accordance with a preferred embodiment of the present invention.

Deconvolution methods are often used in image processing procedures. 5 Examples of such deconvolution methods are described in US Patent 6,166,853 to Sapia et al., the disclosure of which is incorporated herein by reference. (However, it is appreciated that these are just examples and the present invention is not limited to the deconvolution methods mentioned in US Patent 6,166,853)

10 In typical image acquisition, light (or other electromagnetic wave energy) passes through a finite aperture to an image plane. The acquired image is a result of a convolution of the source object's light with the aperture of the imaging system. A system transfer-function may be generally obtained directly by taking the Fourier transform of the aperture. As is known in the art, the 15 blurring effects due to convolution generally exist in two-dimensions only, i.e., the x-y planes. A point-spread-function (PSF) is an expression used to describe the convolutional blurring in two-dimensions. The PSF physically results from imaging a point source. The Fourier transform of the PSF is the system transfer-function, which is obtained by convolving the system transfer-function 20 with a Dirac-delta function. A point source is the physical equivalent of a Dirac-delta function, and, in the frequency domain, the Dirac-delta function is a unity operator across the spectrum. Therefore, the Fourier transform of the PSF should be the Fourier transform of the aperture. However, the PSF contains noise and blurring due to other effects such as aberrations.

25 The PSF contribution to the overall blurriness may be diminished or eliminated by deconvolution.

Referring to Figure 22, in the case of the present invention, the transfer function of the radiation detector may be determined by taking the Fourier transform of the aperture of the detector, and taking into account the noise and 30 blurring due to other effects such as aberrations (step 500). An example of a

60  
transfer function may be a normal distribution. Using known mathematical techniques, the deconvolution of the transfer function may be determined (step 502).

The count readings of each spatial location of the detector constitute the  
5 sum of radiation counts from all the voxels (or pixels in the case of two-dimensional maps, the term "voxel" being used herein to include both pixels and voxels) within the detector's field of view. At least one voxel, or preferably each such voxel, may be assigned a count value based on the deconvolution of the unique transfer function of the radiation detector in use  
10 (step 504). An additional mathematical procedure may treat the various values that each voxel receives due to the multiple readings from viewpoints of different detectors (step 506). This treatment may constitute for example a simple algebraic average, minimum value or reciprocal of averaged reciprocals in order to produce a single value of readings in each voxel. The deconvolution  
15 is then used to reconstruct the voxels of the radiation map with diminished or no blurriness (step 508).

The algorithms described herein are applicable not only to the analysis of readings obtained using a directional radioactivity detector, rather they also apply for spatially sensitive (pixelated) radioactivity detectors. In this case, the  
20 readings of each pixel are algorithmically treated as described herein like for a directional radioactivity detector. The motivation behind using a spatially sensitive detector is to save on measurement time by receiving readings from a multitude of directions in parallel. This, in essence, creates a number of overlapping low resolution images which can then be processed to form a high  
25 resolution image. In addition, the spatially sensitive detector can be scanned to improve even further the resolution using the algorithms described hereinabove.

Thus, the same algorithms that apply for a directional detector apply for the spatially sensitive detector, only now instead of one radiation reading at each position, a large set of discrete positions are processed in parallel. Each pixel

61

can be seen as a separate detector with an angle of acceptance dictated by the geometry of a segmented collimator employed thereby. Each of the pixels occupies a different position in space and hence can be seen as a new position of a single directional probe by the algorithm described herein. It is also possible, like with the directional detector, to scan the whole set of pixels by scanning the spatially sensitive detector and to acquire a new set of data points from the new position. Once obtaining a low resolution image from each of the pixels of the spatially sensitive detector, a super resolution algorithm can be employed to generate an image of higher resolution. Suitable super resolution algorithms are described in, for example, J. Acoust. Soc. Am., Vol. 77, No. 2, February 1985 Pages 567 - 572; Yokota and Sato, IEEE Trans. Acoust. Speech Signal Process. (April 1984); Yokota and Sato, Acoustical Imaging (Plenum, New York, 1982, Vol. 12; H. Shekarforoush and R. Chellappa, "Data-Driven Multi-channel Super-resolution with Application to Video Sequences", Journal of Optical Society of America-A, vol. 16, no. 3, pp. 481-492, 1999; H. Shekarforoush, J. Zerubia and M. Berthod, "Extension of Phase Correlation to Sub-pixel Registration", IEEE Trans. Image Processing, to appear; P. Cheeseman, B. Kanefsky, R. Kraut, J. Stutz, and R. Hanson, "Super-Resolved Surface Reconstruction From Multiple Images," NASA Technical Report FIA-94-12, December, 1994; A.M. Tekalp, M.K. Ozkan, and M.I. Sezan, "High-Resolution Image Reconstruction for Lower-Resolution Image Sequences and Space-Varying Image Restoration," IEEE International Conference on Acoustics, Speech, and Signal Processing (San Francisco, CA), pp. III-169-172, March 23-26, 1992, 25 <http://www-visl.technion.ac.il/1999/99-03/www/>, which are incorporated herein by reference.

#### EXPERIMENTAL RESULTS

In a series of clinical experiments, some of the basic concepts of the invention have been tested on patients who were pre-injected with a suitable

62

radiopharmaceutical for their particular pathology. Two-dimensional color-coded maps have been constructed based on a scan of a pre-determined lesion area by a hand-held radiation detector with a magnetic position-tracking system. The resulting maps, which represented the radiation count level, were 5 compared to images of conventional gamma camera. The list of radiopharmaceuticals tested includes  $^{18}\text{FDG}$ ,  $^{99\text{M}}\text{Tc-MDP}$ ,  $^{99\text{M}}\text{Tc}$  sodium pertechnetate,  $^{99\text{M}}\text{Tc}$  erythrocytes. Similar radiolabeled patterns were observed in the images produced by the system of the invention and in the images produced by a conventional gamma camera in the following pathologies:

10 Figures 23A and 23B illustrate radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of an autonomous adenoma of a thyroid of a 58 year-old male.

15 Figures 24A and 24B illustrate radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of suspected Paget's disease of a humerus in an 89 year-old female.

Figures 25A and 25B illustrate radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of chronic osteomyelitis in a 19 year-old female.

20 Figures 26A and 26B illustrate radiolabeled patterns observed in images produced by the system of the invention and by a conventional gamma camera, respectively, of skeletal metastasis from medulloblastoma in an 18 year-old male.

25 The following provides a list of known procedures which can take advantage of the system and method of the present invention:

In cancer diagnosis the system and method of the present invention can find uses for screening for cancer and/or directing invasive diagnosis (biopsies) either from outside the body or by way of endoscopic approach. Examples include, but are not limited to, lung cancer biopsy, breast cancer biopsy, prostate 30 cancer biopsy, cervical cancer biopsy, liver cancer biopsy, lymph node cancer

63

biopsy, thyroid cancer biopsy, brain cancer biopsy, bone cancer biopsy, colon cancer biopsy, gastro intestine cancer endoscopy and biopsy, endoscopic screening for vaginal cancer, endoscopic screening for prostate cancer (by way of the rectum), endoscopic screening for ovarian cancer. (by way of the vagina),  
5 endoscopic screening for cervical cancer (by way of the vagina), endoscopic screening for bladder cancer (by way of the urinary track), endoscopic screening for bile cancer (by way of the gastrointestinal track), screening for lung cancer, screening for breast cancer, screening for melanoma, screening for brain cancer, screening for lymph cancer, screening for kidney cancer, screening for gastro  
10 intestinal cancer (from the outside).

In the special case of MRI, the radiation detector can be combined and packaged together with a small RF coil for the transmission and reception or reception only of the MRI signals in a rectal probe configuration for prostate diagnosis and treatment or any other close confinement position such as the  
15 vagina, airways, the upper portion of the gastrointestinal track, etc)

Procedures known as directing localized treatment of cancer can also benefit from the system and method of the present invention. Examples include, but are not limited to, intra tumoral chemotherapy, intra tumoral brachytherapy, intra  
20 tumoral cryogenic ablation, intra tumoral radio frequency ablation, intra tumoral ultrasound ablation, and intra tumoral laser ablation, in cases of, for example, lung cancer, breast cancer, prostate cancer, cervical cancer, liver cancer, lymph cancer, thyroid cancer, brain cancer, bone cancer, colon cancer (by way of endoscopy through the rectum), gastric cancer (by way of endoscopy through the thorax), thoracic cancer, small intestine cancer (by way of  
25 endoscopy through the rectum or, by way of endoscopy through the thorax), bladder cancer, kidney cancer, vaginal cancer and ovarian cancer.

In interventional cardiology the following procedures can take advantage of the present invention wherein the method and system can be used to assess tissue perfusion, tissue viability and blood flow intra operatively during PTCA  
30 procedure (balloon alone or in conjunction with the placement of a stent), in

64

cases of cardiogenic shock to asses damage to the heart, following myocardial infarct to asses damage to the heart, in assessing heart failure condition tissue in terms of tissue viability and tissue perfusion, in intra vascular tissue viability and perfusion assessment prior to CABG operation.

5       The radioactivity detector can be mounted on a catheter that is entered through the blood vessels to the heart to evaluate ischemia from within the heart in order to guide ablation probes or another type of treatment to the appropriate location within the heart. Another application which may benefit from the present invention is the localization of blood clots. For example, a radioactivity detector as described herein can be used to asses and differentiate between new clots and old clots. Thus, for example, the radioactivity detector can be placed on a very small caliber wire such as a guide wire that is used during PTCA in order to image intrabloodvessel clots. Intrabloodvessel clots can be searched for in the aortic arc as clots therein are responsible for about 75 % of stroke cases.

10     Using the method and system of the present invention to assess tissue perfusion, tissue viability and blood flow intra operatively can also be employed in the following: during CABG operation to asses tissue viability, to mark infarct areas, during CABG operations to asses the success of the revascularization.

15     The present invention has many other applications in the direction of therapeutics, such as, but not limited to, implanting brachytherapy seeds, ultrasound microwave radio-frequency cryotherapy and localized radiation ablations.

20     It will be appreciated that many other procedures may also take advantage of the present invention.

25     It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the

65  
invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

5        Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications in printed or  
10      electronic form, patents and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall  
15      not be construed as an admission that such reference is available as prior art to the present invention.

## WHAT IS CLAIMED IS:

1. A system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising:
  - (a) a radioactive emission detector;
  - (b) a position tracking system being connected to and/or communicating with said radioactive emission detector; and
  - (c) a data processor being designed and configured for receiving data inputs from said position tracking system and from said radioactive emission detector and for calculating the position of the radioactivity emitting source in the system-of-coordinates.
2. The system of claim 1, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.
3. The system of claim 1, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.
4. The system of claim 1, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a

radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

5. A method for defining a position of a radioactivity emitting source in a system-of-coordinates, the method comprising the steps of:

- (a) providing a radioactive emission detector being connected to or communicating with a position tracking system; and
- (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of said radioactive emission detector in the system-of-coordinates, thereby defining the position of the radioactivity emitting source in the system-of-coordinates.

6. The method for claim 5, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

7. The method for claim 5, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

8. The method for claim 5, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a

radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

9. A system for calculating a position of a radioactivity emitting source in a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising:

- (a) a radioactive emission detector;
- (b) a position tracking system being connected to and/or communicating with said radioactive emission detector; and
- (c) a data processor being designed and configured for:
  - (i) receiving data inputs from said position tracking system and from said radioactive emission detector;
  - (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; and
  - (iii) projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

10. The system of claim 9, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

11. The system of claim 9, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

69

12. The system of claim 9, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

13. A method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the method comprising the steps of:

- (a) providing a radioactive emission detector being connected to or communicating with a position tracking system; and
- (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of said radioactive emission detector in the first system-of-coordinates, thereby defining the position of the radioactivity emitting source in the first system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

14. The method for claim 13, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

15. The method for claim 13, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive

70

emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

16. The method for claim 13, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

17. A system for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the system comprising:

- (a) a three-dimensional imaging modality being connected to and/or communicating with a first position tracking system for calculating the position of the body component in a first system-of-coordinates;
- (b) a radioactive emission detector being connected to and/or communicating with a second position system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and
- (c) at least one data processor being designed and configured for receiving data inputs from said three-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

71

18. The system of claim 17, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said second system-of-coordinates is projected onto said first system-of-coordinates.

19. The system of claim 17, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the body component in said first system-of-coordinates is projected onto said second system-of-coordinates.

20. The system of claim 17, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

21. The system of claim 17, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the body component in said first system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said second system-of-coordinates are both projected onto said common system-of-coordinates.

22. The system of claim 17, wherein said first position tracking system and said second position tracking system are a single position tracking system.

23. The system of claim 17, wherein said imaging modality communicates with an image presentation device which serves for visual co-presentation of said body component and said radiopharmaceutical uptaking portion of the body component.

<sup>72</sup>

24. The system of claim 17, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

25. The system of claim 17, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

26. The system of claim 17, wherein said imaging modality is selected from the group consisting of a Fluoroscope, a Computed Tomographer, an Magnetic Resonance Imager, an ultrasound imager and an optical camera.

27. The system of claim 17, wherein said radiopharmaceutical is selected from the group consisting of <sup>131</sup>I, <sup>67</sup>Ga, <sup>99m</sup>Tc methoxyisobutyl isonitrile, <sup>201</sup>TlCl, <sup>18</sup>F-fluorodeoxyglucose, <sup>125</sup>I-fibrinogen and <sup>111</sup>In-octreotide.

28. A method for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the method comprising the steps of:

- (a) providing a three-dimensional imaging modality being connected to and/or communicating with a first position tracking system and calculating the position of the body component in a first system-of-coordinates;
- (b) providing a radioactive emission detector being connected to and/or communicating with a second position tracking system and

73

tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and

- (c) receiving data inputs from said three-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

29. The method for claim 28, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said second system-of-coordinates is projected onto said first system-of-coordinates.

30. The method for claim 28, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the body component in said first system-of-coordinates is projected onto said second system-of-coordinates.

31. The method for claim 28, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

32. The method for claim 28, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the body component in said first system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said second system-of-coordinates are both projected onto said common system-of-coordinates.

<sup>74</sup>

33. The method for claim 28, wherein said first position tracking system and said second position tracking system are a single position tracking system.

34. The method for claim 28, wherein said imaging modality communicates with an image presentation device which serves for visual co-presentation of said body component and said radiopharmaceutical uptaking portion of the body component.

35. The method for claim 28, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

36. The method for claim 28, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

37. The method for claim 28, wherein said imaging modality is selected from the group consisting of a fluoroscope, a computerized tomography scanner, a magnetic resonance imager and an ultrasound imager and an optical camera.

38. The method for claim 28, wherein said radiopharmaceutical is selected from the group consisting of <sup>131</sup>I, <sup>67</sup>Ga, <sup>99m</sup>Tc methoxyisobutyl isonitrile, <sup>201</sup>TlCl, <sup>18</sup>F-fluorodeoxyglucose, <sup>125</sup>I-fibrinogen and <sup>111</sup>In-octreotide.

39. A system for performing an intrabody surgical procedure on a radiopharmaceutical uptaking portion of a body component within a subject, the system comprising:

- (a) a radioactive emission detector being connected to and/or communicating with a first position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a first system-of-coordinates;
- (b) a surgical instrument being connected to and/or communicating with a second position tracking system for tracking a position of said surgical instrument in a second system-of-coordinates; and
- (c) at least one data processor being designed and configured for receiving data inputs from said first position tracking system, said radioactive emission detector and said second position tracking system and for calculating the position of the surgical instrument and the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

40. The system of claim 39, wherein said surgical instrument includes an additional radioactive emission detector, whereas said at least one data processor being further designed and configured for receiving data inputs from said additional radioactive emission detector for refining the position of the radiopharmaceutical uptaking portion of the body component in the common system-of-coordinates.

41. The system of claim 39, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates is projected onto said second system-of-coordinates.

76

42. The system of claim 39, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates is projected onto said first system-of-coordinates.

43. The system of claim 39, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

44. The system of claim 39, wherein said second system-of-coordinates, said first system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates are both projected onto said common system-of-coordinates.

45. The system of claim 39, wherein said first position tracking system and said second position tracking system are a single position tracking system.

46. The system of claim 39, further comprising an image presentation device which serves for visual co-presentation of the position of said surgical instrument and the radiopharmaceutical uptaking portion of the body component.

47. The system of claim 39, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radioactive emission detector and a sensitive radioactivity detector.

48. The system of claim 39, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

49. The system of claim 39, wherein said surgical instrument is selected from the group consisting of laser probe, cardiac catheter, angioplastic catheter, endoscopic probe, biopsy needle, ultrasonic probe, fiber optic scopes, aspiration tubes, laparoscopy probe, thermal probe and suction/irrigation probe. Please add a pointing device for the open surgery application.

50. The system of claim 39, wherein said radiopharmaceutical is selected from the group consisting of  $^{131}\text{I}$ ,  $^{67}\text{Ga}$ ,  $^{99\text{m}}\text{Tc}$  methoxyisobutyl isonitrile,  $^{201}\text{TlCl}$ ,  $^{18}\text{F}$ -fluorodeoxyglucose,  $^{125}\text{I}$ -fibrinogen and  $^{111}\text{In}$ -octreotide.

51. The system of claim 39, further comprising a three-dimensional imaging modality being connected to and/or communicating with a third position tracking system for calculating the position of a body component in a third system-of-coordinates.

52. The system of claim 51, wherein said data processor being further designed and configured for receiving data inputs from said three-dimensional imaging modality and said third position tracking system and for calculating the position of said surgical instrument and the position of the radiopharmaceutical uptaking portion of a body component and the position of said body component in a common system-of-coordinates.

<sup>78</sup>

53. The system of claim 52, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates and said position of said body component in said third system-of-coordinates are projected onto said second system-of-coordinates.

54. The system of claim 52, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore position of the surgical instrument in said second system-of-coordinates and said position of said body component in said third system-of-coordinates are projected onto said first system-of-coordinates.

55. The system of claim 52, wherein said third system-of-coordinates serves as said common system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates are projected onto said third system-of-coordinates.

56. The system of claim 52, wherein said first system-of-coordinates, said second system-of-coordinates, said third system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

57. The system of claim 52, wherein said second system-of-coordinates, said first system-of-coordinates, said third system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates and the position of said body component in said third

79

system-of-coordinates are all projected onto said common system-of-coordinates.

58. The system of claim 51, wherein said first position tracking system, said second position tracking system and said third position tracking system are a single position tracking system.

59. The system of claim 51, further comprising an image presentation device which serves for visual co-presentation of the position of said surgical instrument and the radiopharmaceutical uptaking portion of the body component and said body component.

60. The system of claim 51, wherein said imaging modality is selected from the group consisting of a fluoroscope, a computerized tomography scanner, a magnetic resonance imager and an ultrasound imager and an optical camera.

61. The system of claim 51, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

62. A method for performing an intrabody surgical procedure on a radiopharmaceutical uptaking portion of a body component within a subject, the method comprising the steps of:

- (a) providing a radioactive emission detector being connected to and/or communicating with a first position tracking system and

80

- tracking a position of the radiopharmaceutical uptaking portion of the body component in a first system-of-coordinates;
- (b) providing a surgical instrument being connected to and/or communicating with a second position tracking system and tracking a position of said surgical instrument in a second system-of-coordinates while performing the intrabody surgical procedure; and
  - (c) receiving data inputs from said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the surgical instrument and the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates while performing the intrabody surgical procedure.

63. The system of claim 62, wherein said surgical instrument includes an additional radioactive emission detector, whereas said at least one data processor being further designed and configured for receiving data inputs from said additional radioactive emission detector for refining the position of the radiopharmaceutical uptaking portion of the body component in the common system-of-coordinates.

64. The method for claim 62, wherein said second system-of-coordinates serves as said common system-of coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates is projected onto said second system-of-coordinates.

65. The method for claim 62, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the

surgical instrument in said second system-of-coordinates is projected onto said first system-of-coordinates.

66. The method for claim 62, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

67. The method for claim 62, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates are both projected onto said common system-of-coordinates.

68. The method for claim 62, wherein said first position tracking system and said second position tracking system are a single position tracking system.

69. The method for claim 62, further comprising an image presentation device which serves for visual co-presentation of the position of said surgical instrument and the radiopharmaceutical uptaking portion of the body component.

70. The method for claim 62, wherein said radioactive emission detector is selected from the group consisting of a narrow angle radioactive emission detector, a wide angle radiation emission detector, a plurality of individual narrow angle radiation emission detectors and a spatially sensitive radioactivity detector.

<sup>82</sup>

71. The method for claim 62, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometer based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system

72. The method for claim 62, wherein said surgical instrument is selected from the group consisting of laser probe, cardiac catheter, angioplastics catheter, endoscopic probe, biopsy needle, ultrasonic probe, fiber optic scopes, aspiration tubes, laparoscopy probe, thermal probe and suction/irrigation probe.

73. The method for claim 62, wherein said radiopharmaceutical is selected from the group consisting of <sup>131</sup>I, <sup>67</sup>Ga, <sup>99M</sup>Tc methoxyisobutyl isonitrile, <sup>201</sup>TlCl, <sup>18</sup>F-fluorodeoxyglucose, <sup>125</sup>I-fibrinogen and <sup>111</sup>In-octreotide.

74. The method for claim 62, further the step of providing a three-dimensional imaging modality being connected to and/or communicating with a third position tracking system and calculating the position of a body component in a third system-of-coordinates.

75. The method for claim 74, further comprising the step of receiving data inputs from said three-dimensional imaging modality and said third position tracking system and for calculating the position of said surgical instrument and the position of the radiopharmaceutical uptaking portion of a body component and the position of said body component in a common system-of-coordinates.

<sup>83</sup>

76. The method for claim 74, wherein said first position tracking system, said second position tracking system and said third position tracking system are a single position tracking system.

77. The method for claim 74, further comprising the step of co-presenting the position of said surgical instrument and the radiopharmaceutical uptaking portion of the body component and said body component via a visual presentation device.

78. The method for claim 74, wherein said imaging modality is selected from the group consisting of a fluoroscope, a computerized tomography scanner, a magnetic resonance imager and an ultrasound imager and an optical camera.

79. The method for claim 74, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system

80. The method for claim 75, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates and said position of said body component in said third system-of-coordinates are projected onto said second system-of-coordinates.

81. The method for claim 75, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the

84

surgical instrument in said second system-of-coordinates and said position of said body component in said third system-of-coordinates are projected onto said first system-of-coordinates.

82. The method for claim 75, wherein said third system-of-coordinates serves as said common system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates are projected onto said third system-of-coordinates.

83. The method for claim 75, wherein said first system-of-coordinates, said second system-of-coordinates, said third system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

84. The method for claim 75, wherein said first system-of-coordinates, said second system-of-coordinates, said third system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the surgical instrument in said second system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component in said first system-of-coordinates and the position of said body component in said third system-of-coordinates are all projected onto said common system-of-coordinates.

85. A system for generating a two- or three-dimensional image of a radioactivity emitting source in a body, the system comprising:

- (a) a radioactive emission detector;

85

- (b) a position tracking system being connected to and/or communicating with said radioactive emission detector; and
- (c) a data processor being designed and configured for receiving data inputs from said position tracking system and from said radioactive emission detector and for generating the two- or three-dimensional image of the radioactivity emitting source.

86. A method of generating a two- or three-dimensional image of a radioactivity emitting source in a body, the system comprising:

- (a) scanning the body with a radioactive emission detector;
- (b) using a position tracking system being connected to and/or communicating with said radioactive emission detector for determining a position in a three-dimensional system of coordinates of said radioactive emission detector; and
- (c) data processing inputs from said position tracking system and from said radioactive emission detector for generating the two- or three-dimensional image of the radioactivity emitting source.

87. A system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising:

- (a) at least two radioactive emission detectors;
- (b) a position tracking system being connected to and/or communicating with said at least two radioactive emission detectors; and
- (c) a data processor being designed and configured for receiving data inputs from said position tracking system and from said at least two radioactive emission detectors and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

86

88. The system of claim 87, wherein said at least two radioactive emission detectors are physically connected therebetween via a flexible connector.

89. A method for defining a position of a radioactivity emitting source in a system-of-coordinates, the method comprising the steps of:

- (a) providing at least one radioactive emission detector being connected to or communicating with a position tracking system; and
- (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of said at least one radioactive emission detector in the system-of-coordinates, thereby defining the position of the radioactivity emitting source in the system-of-coordinates.

90. The method of claim 89, wherein at least two radioactive emission detectors are provided.

91. The method of claim 90, wherein said at least two radioactive emission detectors are physically connected therebetween via a flexible connector.

92. A system for calculating a position of a radioactivity emitting source in a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising:

- (a) at least two radioactive emission detectors;
- (b) a position tracking system being connected to and/or communicating with said at least two radioactive emission detectors; and

- 87
- (c) a data processor being designed and configured for:
- (i) receiving data inputs from said position tracking system and from said at least two radioactive emission detectors;
  - (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates; and
  - (iii) projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

93. The system of claim 92, wherein said at least two radioactive emission detectors are physically connected therebetween via a flexible connector.

94. A method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of, the method comprising the steps of:

- (a) providing at least one radioactive emission detector being connected to or communicating with a position tracking system; and
- (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of said at least one radioactive emission detector in the first system-of-coordinates, thereby defining the position of the radioactivity emitting source in the first system-of-coordinates and projecting the position of the radioactivity emitting source onto the second system-of-coordinates.

95. A system for performing an intrabody surgical procedure on a radiopharmaceutical uptaking portion of a body component within a subject, the system comprising a surgical instrument being connected to and/or

communicating with a position tracking system for tracking a position of said surgical instrument in a system-of-coordinates, said surgical instrument including a radioactive emission detector coupled thereto for monitoring said radiopharmaceutical in situ.

96. The system of claim 95, wherein said radioactive emission detector is sensitive to beta radiation and/or positron radiation.

97. The system of claim 95, wherein said surgical instrument includes a tissue resecting mechanism.

98. The system of claim 95, wherein said surgical instrument includes a tissue sampling mechanism.

99. The system of claim 95, wherein said tissue sampling mechanism includes an aspiration mechanism.

100. A system for calculating a position of a radioactivity emitting source in a system-of-coordinates, the system comprising:

- (a) a surgical instrument designed and constructed for invading a body of a subject, said surgical instrument including a radioactive emission detector connected thereto or integrated therein;
- (b) a position tracking system being connected to and/or communicating with said surgical instrument; and
- (c) a data processor being designed and configured for receiving data inputs from said position tracking system and from said radioactive emission detector and for calculating the position of the radioactivity emitting source in the system-of-coordinates.

89

101. The system of claim 100, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

102. The system of claim 100, wherein said radioactive emission detector is a narrow angle radioactive emission detector or a wide angle radioactive emission detector.

103. The system of claim 100, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

104. A system for calculating a position of a radioactivity emitting source in a first system-of-coordinates and further of projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the system comprising:

- (a) a surgical instrument designed and constructed for invading a body of a subject, said surgical instrument including a radioactive emission detector connected thereto or integrated therein;
- (b) a position tracking system being connected to and/or communicating with said surgical instrument; and
- (c) a data processor being designed and configured for:
  - (i) receiving data inputs from said position tracking system and from said radioactive emission detector;

90

- (ii) calculating the position of the radioactivity emitting source in the first system-of-coordinates;
- (iii) calculating the position of said surgical instrument in the first system-of-coordinates; and
- (iii) projecting the position of the radioactivity emitting source and of the surgical instrument onto the second system-of-coordinates.

105. The system of claim 104, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

106. The system of claim 104, wherein said radioactive emission detector is a narrow angle radioactive emission detector or a wide angle radioactive emission detector.

107. The system of claim 104, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

108. A method for calculating a position of a radioactivity emitting source in a first system-of-coordinates and for projecting the position of the radioactivity emitting source onto a second system-of-coordinates, the method comprising the steps of:

91

- (a) providing a surgical instrument designed and constructed for invading a body of a subject, said surgical instrument including a radioactive emission detector connected thereto or integrated therein, said surgical instrument being connected to or communicating with a position tracking system; and
- (b) monitoring radioactivity being emitted from the radioactivity emitting source, while at the same time, monitoring the position of said radioactive emission detector in the first system-of-coordinates, thereby defining the positions of the radioactivity emitting source and of the surgical instrument in the first system-of-coordinates and the position of the radioactivity emitting source onto the second system-of-coordinates.

109. The method for claim 108, wherein the radioactivity emitting source is selected from the group consisting of a radiopharmaceutically labeled benign tumor, a radiopharmaceutically labeled malignant tumor, a radiopharmaceutically labeled vascular clot, radiopharmaceutically labeled inflammation related components, a radiopharmaceutically labeled abscess and a radiopharmaceutically labeled vascular abnormality.

110. The method for claim 108, wherein said radioactive emission detector is a narrow angle radioactive emission detector or a wide angle radioactive emission detector.

111. The method for claim 108, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

92

112. A system for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the system comprising:

- (a) a three-dimensional imaging modality being connected to and/or communicating with a first position tracking system for calculating the position of the body component in a first system-of-coordinates;
- (b) a surgical instrument designed and constructed for invading the body, said surgical instrument including a radioactive emission detector connected thereto or integrated therein, said surgical instrument being connected to and/or communicating with a second position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and
- (c) at least one data processor being designed and configured for receiving inputs from said three-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component, the position of the radiopharmaceutical uptaking portion of the body component and the position of the surgical instrument in a common system-of-coordinates.

113. The system of claim 112, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the position of the radiopharmaceutical uptaking portion of the body component in said second system-of-coordinates is projected onto said first system-of-coordinates.

114. The system of claim 112, wherein said second system-of-coordinates serves as said common system-of-coordinates and

93

therefore the position of the body component and surgical device in said first system-of-coordinates is projected onto said second system-of-coordinates.

115. The system of claim 112, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

116. The system of claim 112, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the body component in said first system-of-coordinates and the positions of the radiopharmaceutical uptaking portion of the body component and of said surgical instrument in said second system-of-coordinates are projected onto said common system-of-coordinates.

117. The system of claim 112, wherein said first position tracking system and said second position tracking system are a single position tracking system.

118. The system of claim 112, wherein said imaging modality communicates with an image presentation device which serves for visual co-presentation of said body component and said radiopharmaceutical uptaking portion of the body component.

119. The system of claim 112, wherein said radioactive emission detector is a narrow angle radioactive emission detector or a wide angle radioactive emission detector.

120. The system of claim 112, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking

94

system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

121. The system of claim 112, wherein said imaging modality is selected from the group consisting of a Fluoroscope, a Computed Tomographer, an Magnetic Resonance Imager, an ultrasound imager and an optical camera.

122. The system of claim 112, wherein said radiopharmaceutical is selected from the group consisting of 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose, <sup>111</sup>In-Pentetreotide, L-3-[<sup>123</sup>I]-Iodo-alpha-methyl-tyrosine, O-(2-[<sup>18</sup>F]fluoroethyl)-L-tyrosine, <sup>111</sup>In-Capromab Pendetide and <sup>111</sup>In-Satumomab Pendetide.

123. A method for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the method comprising the steps of:

- (a) providing a three-dimensional imaging modality being connected to and/or communicating with a first position tracking system and calculating the position of the body component in a first system-of-coordinates;
- (b) providing a surgical instrument designed and constructed for invading the body, said surgical instrument including a radioactive emission detector connected thereto or integrated therein, said surgical instrument being connected to and/or communicating with a second position tracking system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and

95

- (c) receiving data inputs from said three-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component, the position of the surgical instrument and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

124. The method for claim 123, wherein said first system-of-coordinates serves as said common system-of-coordinates and therefore the positions of the radiopharmaceutical uptaking portion of the body component and of the surgical instrument in said second system-of-coordinates is projected onto said first system-of-coordinates.

125. The method for claim 123, wherein said second system-of-coordinates serves as said common system-of-coordinates and therefore the position of the body component in said first system-of-coordinates is projected onto said second system-of-coordinates.

126. The method for claim 123, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are a single system-of-coordinates.

127. The method for claim 113, wherein said first system-of-coordinates, said second system-of-coordinates and said common system-of-coordinates are each a separate system-of-coordinates and therefore the position of the body component in said first system-of-coordinates and the position of the radiopharmaceutical uptaking portion of the body component and of said surgical instrument in said second system-of-coordinates are both projected onto said common system-of-coordinates.

96

128. The method for claim 113, wherein said first position tracking system and said second position tracking system are a single position tracking system.

129. The method for claim 113, wherein said imaging modality communicates with an image presentation device which serves for visual co-presentation of said body component, said radiopharmaceutical uptaking portion of the body component and said surgical instrument.

130. The method for claim 113, wherein said radioactive emission detector is a narrow angle radioactive emission detector or a wide angle radioactive emission detector.

131. The method for claim 113, wherein said position tracking system is selected from the group consisting of an articulated arm position tracking system, an accelerometers based position tracking system, a potentiometers based position tracking system, a sound wave based position tracking system, a radio frequency based position tracking system, a magnetic field based position tracking system and an optical based position tracking system.

132. The method for claim 113, wherein said imaging modality is selected from the group consisting of a fluoroscope, a computerized tomography scanner, a magnetic resonance imager and an ultrasound imager and an optical camera.

133. The method for claim 113, wherein said radiopharmaceutical is selected from the group consisting of 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose, <sup>111</sup>In-Pentetreotide, O-(2-[<sup>18</sup>F]fluoroethyl)-L-tyrosine, <sup>111</sup>In-Satumomab Pendetide, L-3-[<sup>123</sup>I]-Iodo-alpha-methyl-tyrosine, <sup>111</sup>In-Capromab Pendetide and <sup>111</sup>In-Capromab Pendetide.

97

134. The system of claim 1, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

135. The system of claim 134, further comprising a memory adapted to store therein said positional information together with said count rate.

136. The system of claim 134, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

137. The system of claim 134, wherein said data processor is adapted to refine said count rate and said positional information.

138. The system of claim 137, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with:  $N(X_c+dx, Y_c+dy,$

98

$$Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \varphi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1].$$

139. The system of claim 137, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

140. The system of claim 9, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

141. The system of claim 140, further comprising a memory adapted to store therein said positional information together with said count rate.

142. The system of claim 140, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

99

143. The system of claim 140, wherein said data processor is adapted to refine said count rate and said positional information.

144. The system of claim 143, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [ N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi) ] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

145. The system of claim 143, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , finding those voxels that have a higher count rate value  $N(X_c+dx, Y_c+dy, Z_c+dz)$  than said detector count

100

rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ .

146. The system of claim 17, wherein said at least one data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

147. The system of claim 146, further comprising a memory adapted to store therein said positional information together with said count rate.

148. The system of claim 146, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

149. The system of claim 146, wherein said at least one data processor is adapted to refine said count rate and said positional information.

150. The system of claim 149, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said at least one data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count

101

rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \phi)]/[M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

151. The system of claim 149, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said at least one data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ .

152. The system of claim 39, wherein said at least one data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

153. The system of claim 152, further comprising a memory adapted to store therein said positional information together with said count rate.

102

154. The system of claim 152, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

155. The system of claim 152, wherein said at least one data processor is adapted to refine said count rate and said positional information.

156. The system of claim 155, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said at least one data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \phi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

157. The system of claim 155, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said at least one data processor is adapted to minimize said count rate

103

and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ .

158. The system of claim 85, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

159. The system of claim 158, further comprising a memory adapted to store therein said positional information together with said count rate.

160. The system of claim 158, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

161. The system of claim 158, wherein said data processor is adapted to refine said count rate and said positional information.

162. The system of claim 161, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further,

<sup>104</sup>

wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , determining  $M(Xc+dx, Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \varphi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

163. The system of claim 161, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

164. The system of claim 87, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

105

165. The system of claim 164, further comprising a memory adapted to store therein said positional information together with said count rate.

166. The system of claim 164, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

167. The system of claim 164, wherein said data processor is adapted to refine said count rate and said positional information.

168. The system of claim 167, wherein said system-of-coordinates comprises mutually perpendicular axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

169. The system of claim 167, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the

106

system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , finding those voxels that have a higher count rate value  $N(X_c+dx, Y_c+dy, Z_c+dz)$  than said detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ .

170. The system of claim 92, wherein said data processor is adapted to combine a radiation detector count rate from said at least two radioactive emission detectors together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

171. The system of claim 170, further comprising a memory adapted to store therein said positional information together with said count rate.

172. The system of claim 170, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

173. The system of claim 170, wherein said data processor is adapted to refine said count rate and said positional information.

174. The system of claim 173, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about

107

the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of at least one of said at least two detectors is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said at least one of said at least two detectors is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

175. The system of claim 173, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of at least one of said at least two detectors is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said at least one of said at least two detectors is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , finding those voxels that have a higher count rate value  $N(X_c+dx, Y_c+dy, Z_c+dz)$  than said detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ .

108

176. The system of claim 95, further comprising a data processor, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

177. The system of claim 176, further comprising a memory adapted to store therein said positional information together with said count rate.

178. The system of claim 176, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

179. The system of claim 176, wherein said data processor is adapted to refine said count rate and said positional information.

180. The system of claim 179, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy,$

109

$$Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \varphi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1].$$

181. The system of claim 179, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

182. The system of claim 100, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

183. The system of claim 18, further comprising a memory adapted to store therein said positional information together with said count rate.

184. The system of claim 182, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

<sup>110</sup>

185. The system of claim 182, wherein said data processor is adapted to refine said count rate and said positional information.

186. The system of claim 185, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \phi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

187. The system of claim 185, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , finding those voxels that have a higher rate value  $N(X_c+dx, Y_c+dy, Z_c+dz)$  than said detector count rate

111

$N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ .

188. The system of claim 104, wherein said data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

189. The system of claim 188, further comprising a memory adapted to store therein said positional information together with said count rate.

190. The system of claim 188, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

191. The system of claim 188, wherein said data processor is adapted to refine said count rate and said positional information.

192. The system of claim 191, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx,$

112

$Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \phi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

193. The system of claim 191, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ .

194. The system of claim 112, wherein said at least one data processor is adapted to combine a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and is adapted to form a radiotracer-spread image of a target area including therein said radioactivity emitting source.

195. The system of claim 194, further comprising a memory adapted to store therein said positional information together with said count rate.

113

196. The system of claim 194, further comprising a display adapted to display thereon said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

197. The system of claim 194, wherein said at least one data processor is adapted to refine said count rate and said positional information.

198. The system of claim 197, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said at least one data processor is adapted to average said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

199. The system of claim 197, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further,

114

wherein said at least one data processor is adapted to minimize said count rate and said positional information by finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

200. The method of claim 5, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

201. The method of claim 200, further comprising storing said positional information together with said count rate in a memory.

202. The method of claim 200, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

203. The method of claim 200, further comprising refining said count rate and said positional information.

204. The method of claim 203, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ ,

115

and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , determining  $M(Xc+dx, Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \phi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

205. The method of claim 203, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ .

206. The method of claim 28, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

116

207. The method of claim 206, further comprising storing said positional information together with said count rate in a memory.

208. The method of claim 206, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

209. The method of claim 206, further comprising refining said count rate and said positional information.

210. The method of claim 209, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \phi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

211. The method of claim 209, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \phi)$ ,

117

and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

212. The method of claim 62, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

213. The method of claim 212, further comprising storing said positional information together with said count rate in a memory.

214. The method of claim 212, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

215. The method of claim 212, further comprising refining said count rate and said positional information.

216. The method of claim 215, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ ,

118

and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , determining  $M(Xc+dx, Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \varphi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

217. The method of claim 215, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

218. The method of claim 86, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

119

219. The method of claim 218, further comprising storing said positional information together with said count rate in a memory.

220. The method of claim 218, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

221. The method of claim 218, further comprising refining said count rate and said positional information.

222. The method of claim 221, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

223. The method of claim 221, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ ,

120

and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

224. The method of claim 89, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

225. The method of claim 224, further comprising storing said positional information together with said count rate in a memory.

226. The method of claim 224, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

227. The method of claim 224, further comprising refining said count rate and said positional information.

228. The method of claim 227, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ ,

121

and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , determining  $M(Xc+dx, Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \varphi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

229. The method of claim 227, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as ( $dx$ ,  $dy$ ,  $dz$ ); and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx$ ,  $Yc+dy$ ,  $Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

230. The method of claim 94, further comprising combining a radiation detector count rate from said at least one radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

231. The method of claim 230, further comprising storing said positional information together with said count rate in a memory.

122

232. The method of claim 230, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

233. The method of claim 230, further comprising refining said count rate and said positional information.

234. The method of claim 233, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said at least one detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said at least one detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

235. The method of claim 233, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said at least one detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said at least one detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy,$

123

$Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

236. The method of claim 108, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

237. The method of claim 236, further comprising storing said positional information together with said count rate in a memory.

238. The method of claim 236, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

239. The method of claim 236, further comprising refining said count rate and said positional information.

240. The method of claim 239, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , determining

124

$M(Xc+dx, Yc+dy, Zc+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(Xc+dx, Yc+dy, Zc+dz) = [N(Xc+dx, Yc+dy, Zc+dz) + N(Xc, Yc, Zc, \rho, \theta, \phi)] / [M(Xc+dx, Yc+dy, Zc+dz) + 1]$ .

241. The method of claim 239, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\phi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(Xc, Yc, Zc, \rho, \theta, \phi)$ , said detector count rate is defined as  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $Xc+dx, Yc+dy, Zc+dz$ , finding those voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \phi)$ .

242. The method of claim 123, further comprising combining a radiation detector count rate from said radioactive emission detector together with positional information from said position tracking system, and forming a radiotracer-spread image of a target area including therein said radioactivity emitting source.

243. The method of claim 242, further comprising storing said positional information together with said count rate in a memory.

<sup>125</sup>

244. The method of claim 242, further comprising displaying said positional information together with said count rate as a pattern of marks corresponding to said positional information and said count rate.

245: The method of claim 242, further comprising refining said count rate and said positional information.

246. The method of claim 245, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , determining  $M(X_c+dx, Y_c+dy, Z_c+dz)$  which represents the number of times that said count rate and said positional information have been calculated in each voxel, and calculating average count rate values in each voxel in accordance with  $N(X_c+dx, Y_c+dy, Z_c+dz) = [N(X_c+dx, Y_c+dy, Z_c+dz) + N(X_c, Y_c, Z_c, \rho, \theta, \varphi)] / [M(X_c+dx, Y_c+dy, Z_c+dz) + 1]$ .

247. The method of claim 245, wherein said system-of-coordinates comprises mutually perpendicular linear axes X, Y and Z, and rotations about the X, Y and Z axes,  $\rho$ ,  $\theta$  and  $\varphi$ , respectively, and wherein in the system-of-coordinates, said positional information of said detector is defined as  $(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , said detector count rate is defined as  $N(X_c, Y_c, Z_c, \rho, \theta, \varphi)$ , and a physical size of said detector is defined as  $(dx, dy, dz)$ ; and further, wherein said refining comprises finding all volume pixels, called voxels, that represent the detector volume, defined as  $X_c+dx, Y_c+dy, Z_c+dz$ , finding those

126

voxels that have a higher count rate value  $N(Xc+dx, Yc+dy, Zc+dz)$  than said detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$  which was input, and changing the higher count rate voxels to that of the inputted detector count rate  $N(Xc, Yc, Zc, \rho, \theta, \varphi)$ .

248. A method for radiation map reconstruction, the method comprising:

- (a) determining a transfer function of a radiation detector;
- (b) determining a deconvolution of said transfer function;
- (c) assigning a count value based on said deconvolution to at least one voxel within a field of view of said radiation detector; and
- (d) using said deconvolution to reconstruct said at least one voxel.

249. The method of claim 248, wherein said using said deconvolution comprises at least diminishing blurriness of said at least one voxel.

250. The method of claim 248, further comprising mathematically treating multiple readings from viewpoints of different detectors that said at least one voxel receives.

251. The method of claim 250, wherein said mathematically treating comprises determining a value used in place of a single value of reading in said at least one voxel.

252. The method of claim 251, wherein said determining a value comprises determining at least one of an algebraic average, a minimum value, and a reciprocal of averaged reciprocals of readings in said at least one voxel.

127

253. A system for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the system comprising:

- (a) a two-dimensional imaging modality being connected to and/or communicating with a first position tracking system for calculating the position of the body component in a first system-of-coordinates;
- (b) a radioactive emission detector being connected to and/or communicating with a second position system for tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and
- (c) at least one data processor being designed and configured for receiving data inputs from said two-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

254. A method for calculating a position of a body component and a position of a radiopharmaceutical uptaking portion of the body component within a subject, the method comprising the steps of:

- (a) providing a two-dimensional imaging modality being connected to and/or communicating with a first position tracking system and calculating the position of the body component in a first system-of-coordinates;
- (b) providing a radioactive emission detector being connected to and/or communicating with a second position tracking system and tracking a position of the radiopharmaceutical uptaking portion of the body component in a second system-of-coordinates; and

128

- (c) receiving data inputs from said two-dimensional imaging modality, said first position tracking system, said radioactive emission detector and said second position tracking system and calculating the position of the body component and the position of the radiopharmaceutical uptaking portion of the body component in a common system-of-coordinates.

1/21

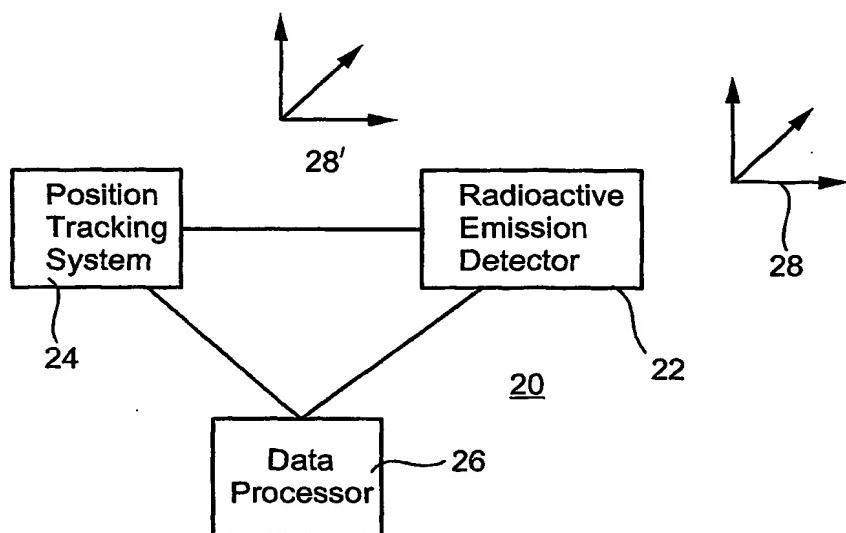


Fig. 1

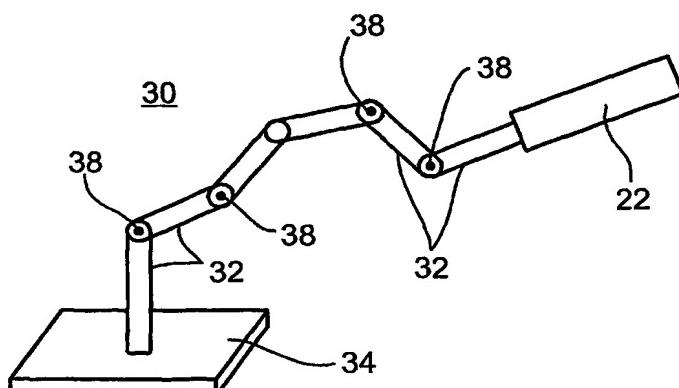


Fig. 2

2/21

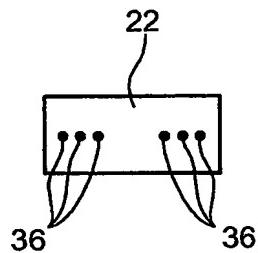


Fig. 3

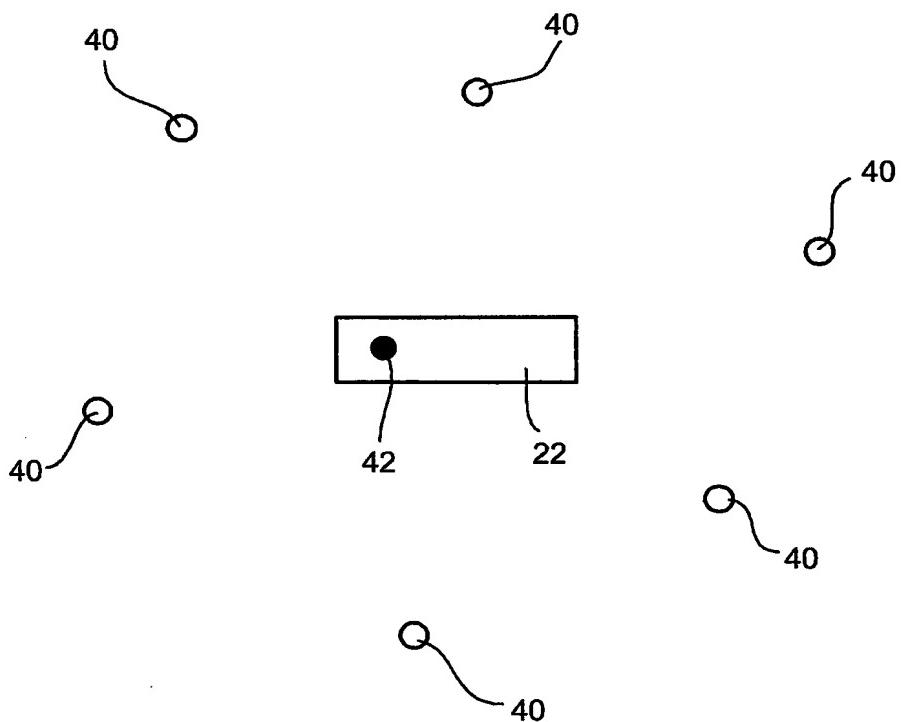


Fig. 4

3/21

22

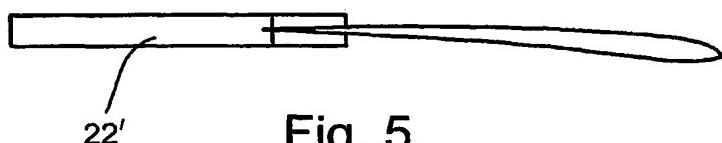


Fig. 5

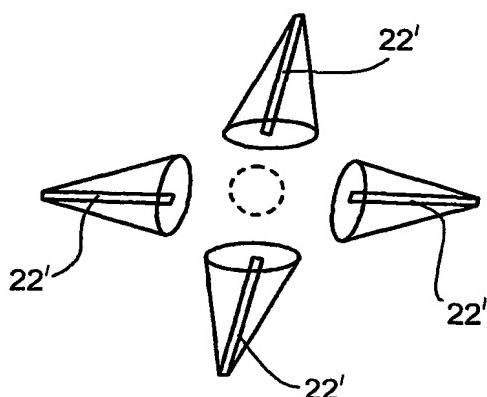


Fig. 6

22

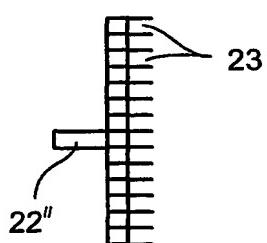


Fig. 7

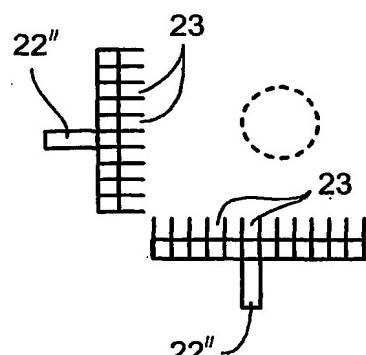


Fig. 8

4/21

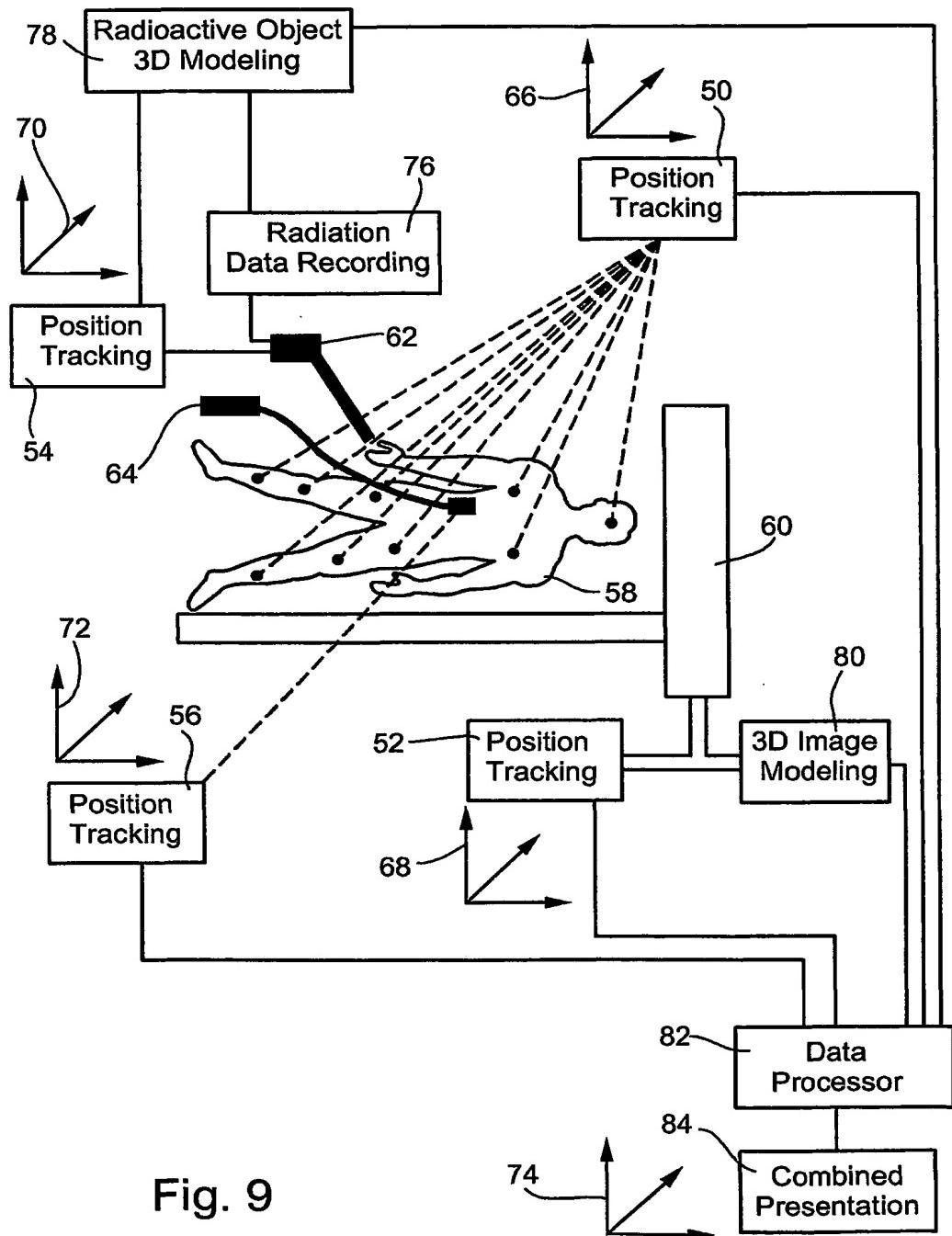


Fig. 9

5/21

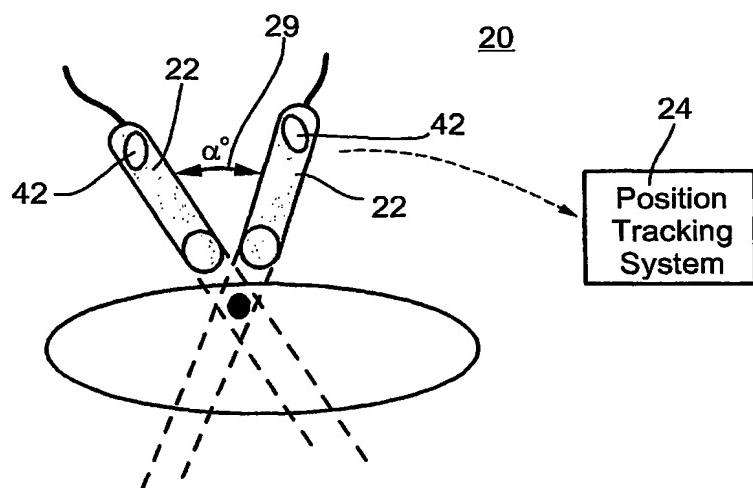


Fig. 10

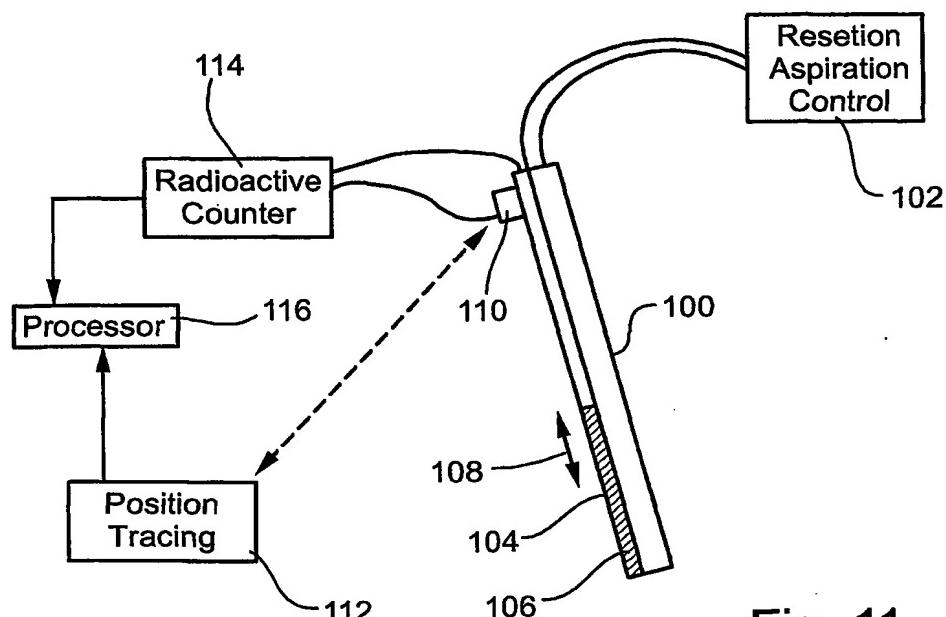


Fig. 11

6/21

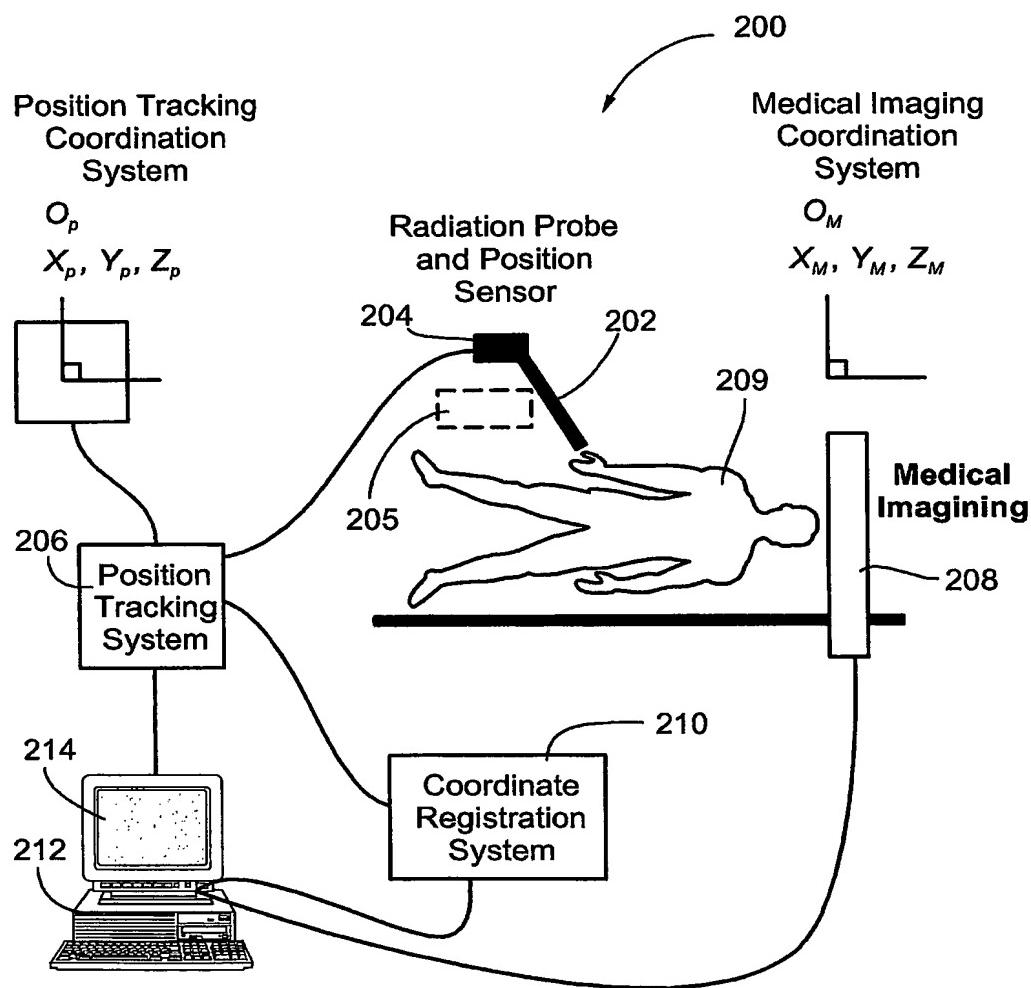


Fig. 12

7/21

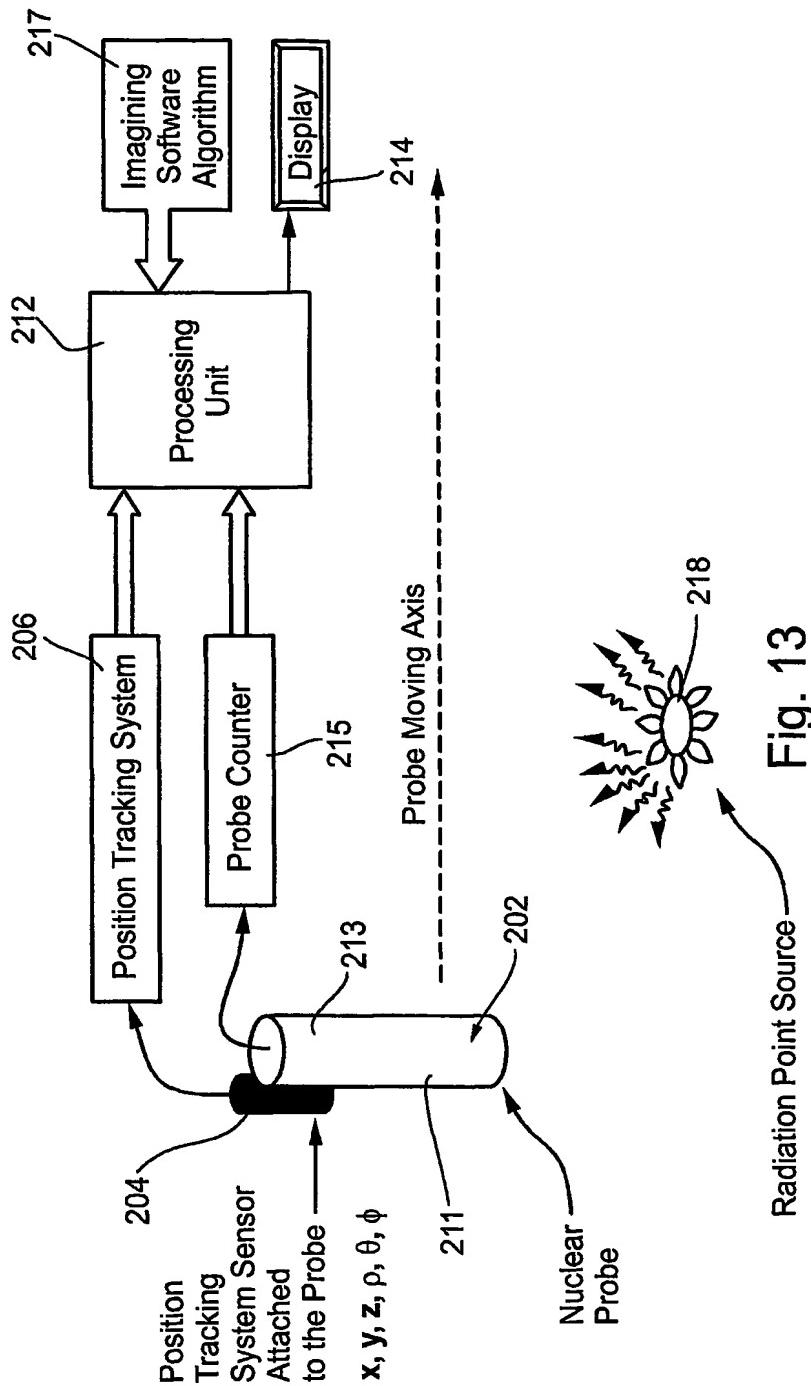


Fig. 13

Radiation Point Source

8/21

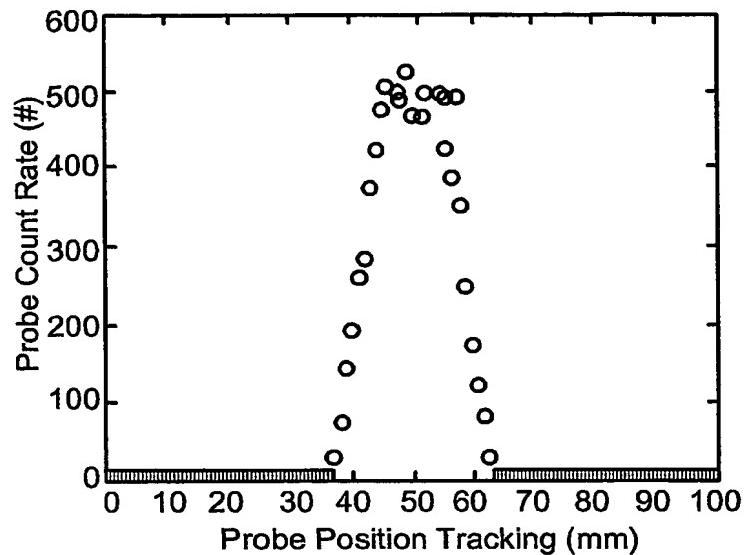


Fig. 14

9/21

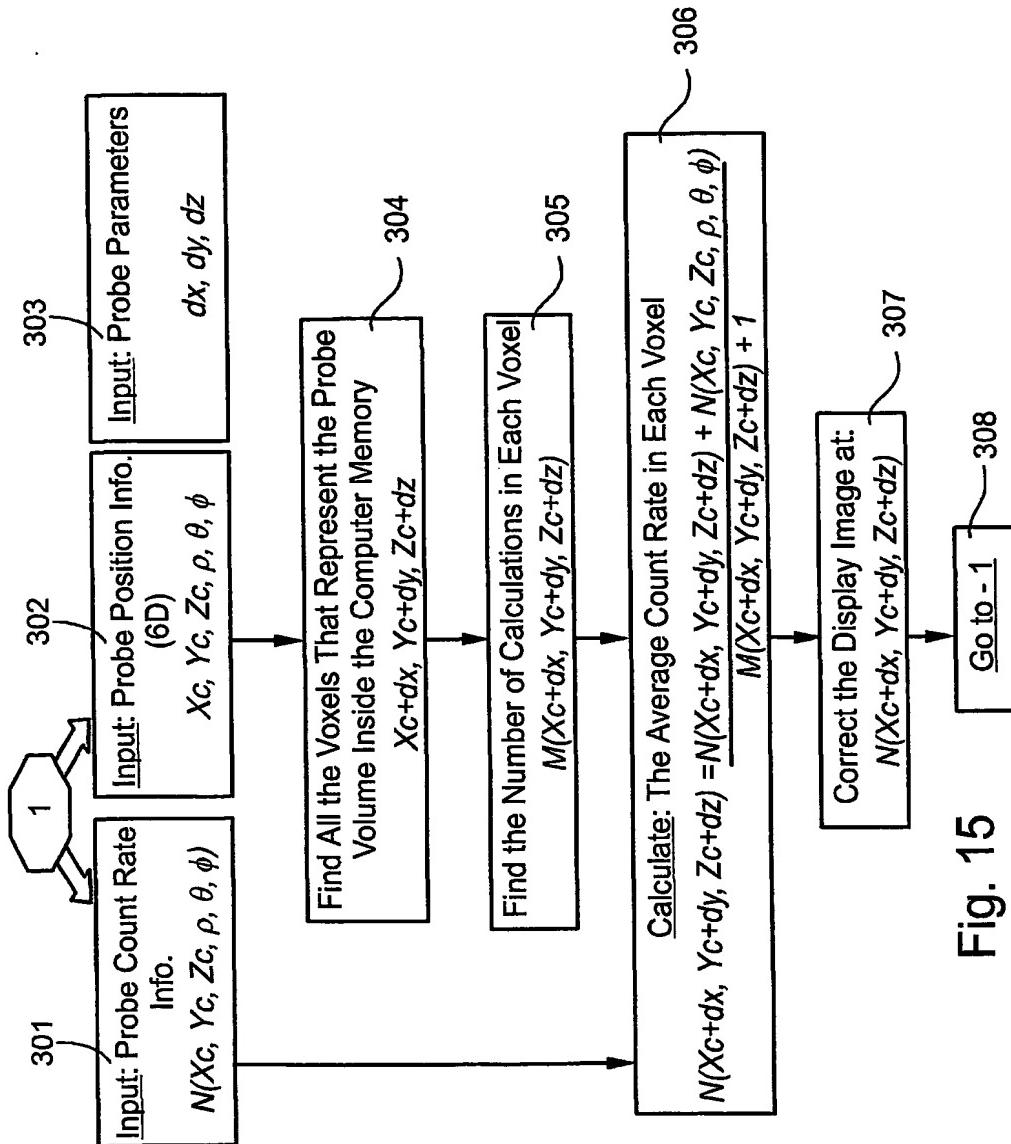


Fig. 15

10/21

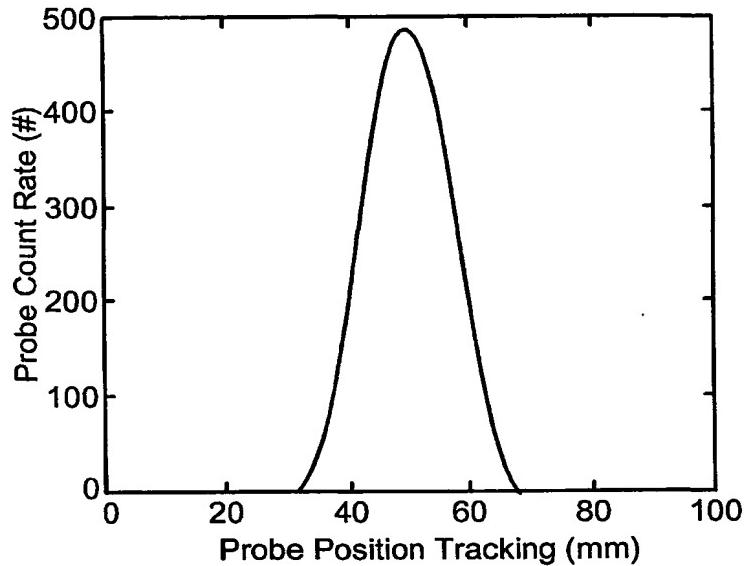


Fig. 16

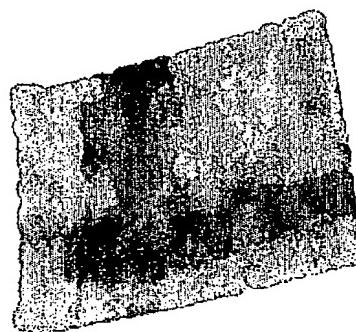


Fig. 17

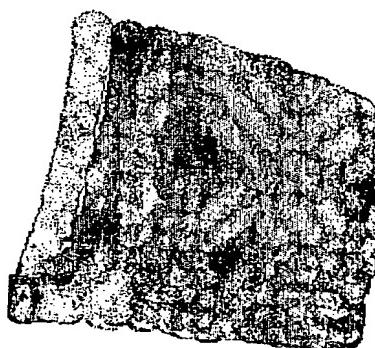


Fig. 18

11/21

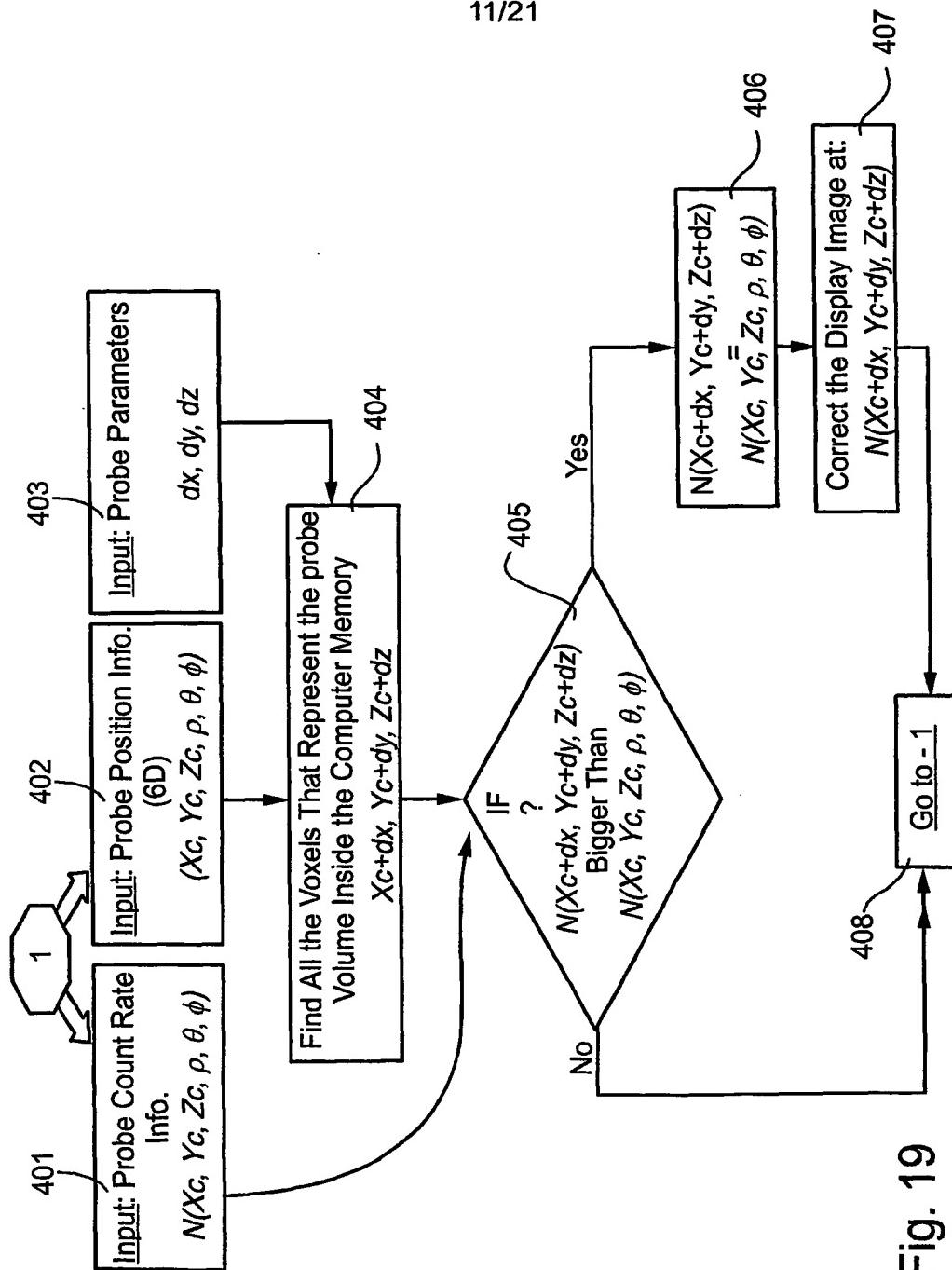


Fig. 19

12/21

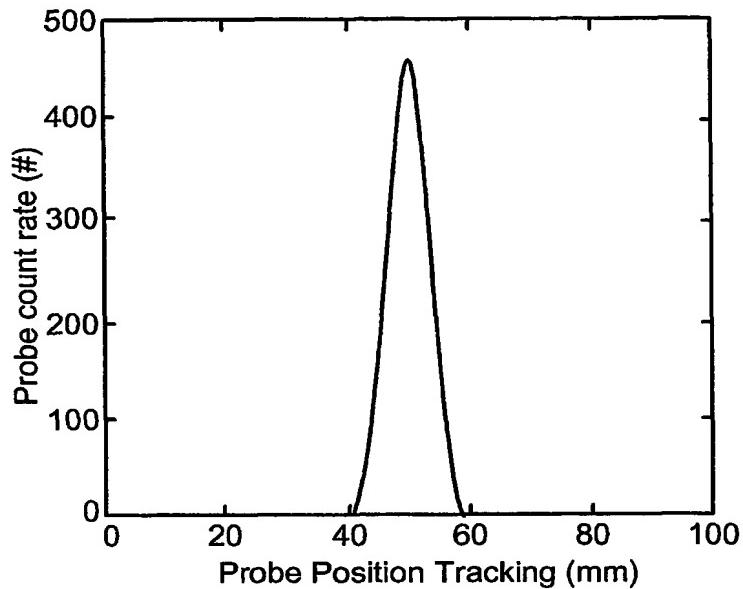


Fig. 20

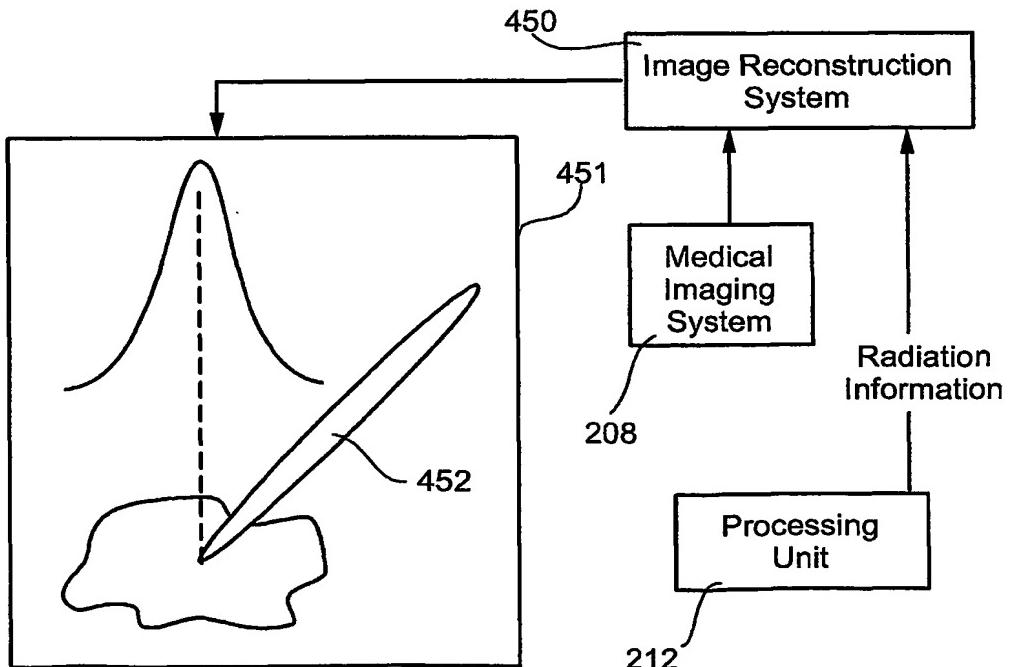


Fig. 21

13/21

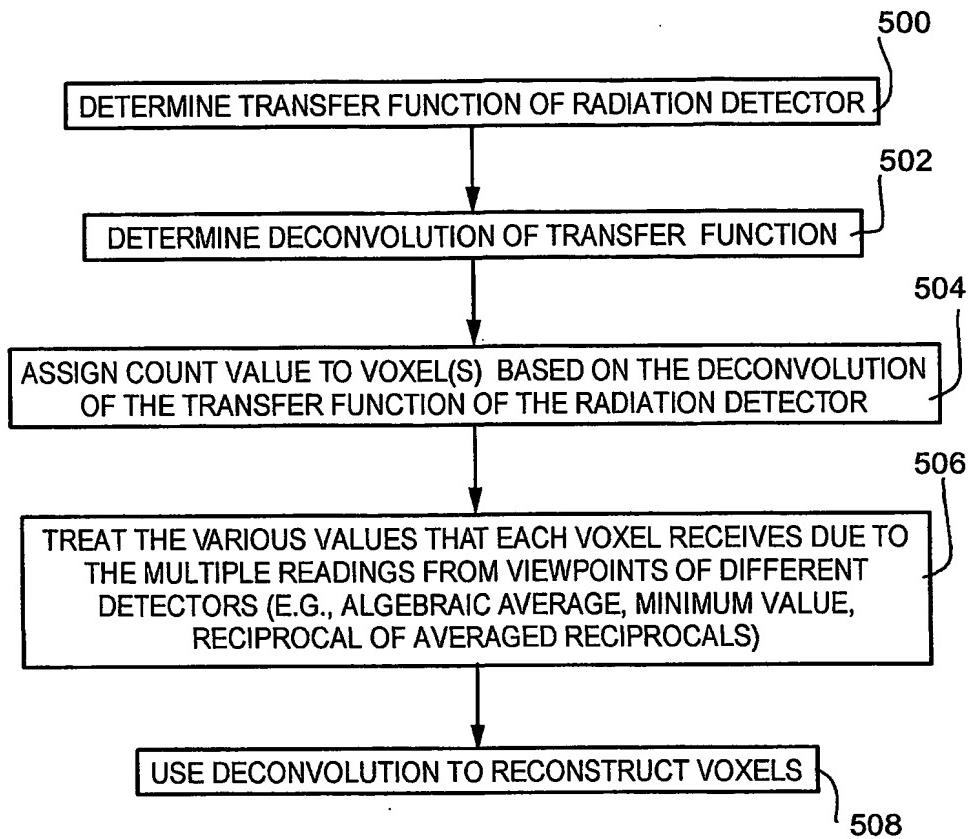


Fig. 22

14/21

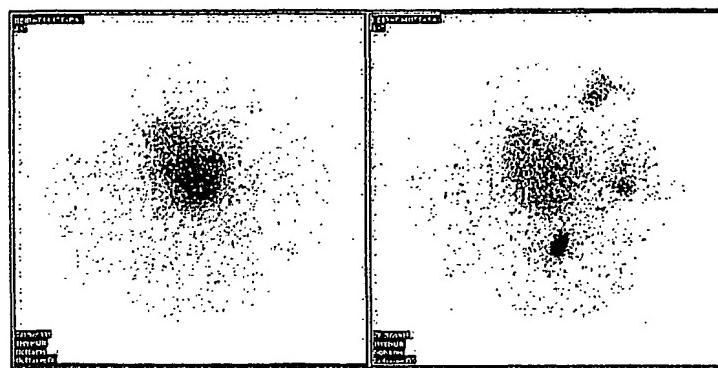


Fig. 23b

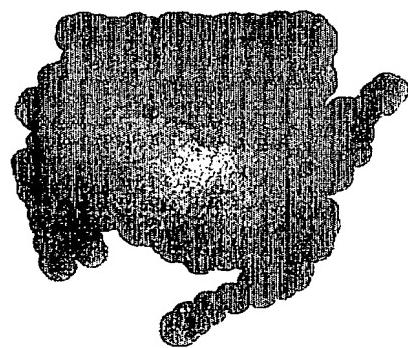


Fig. 23a

15/21

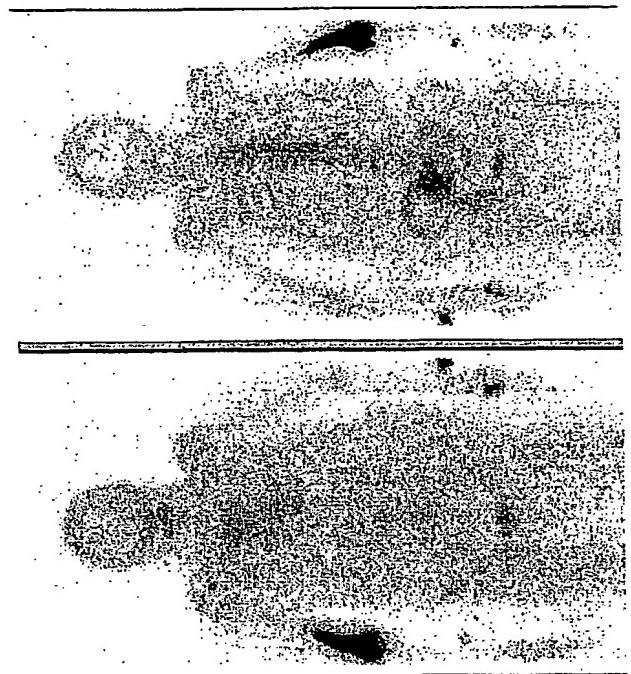


Fig. 24B

Fig. 24b

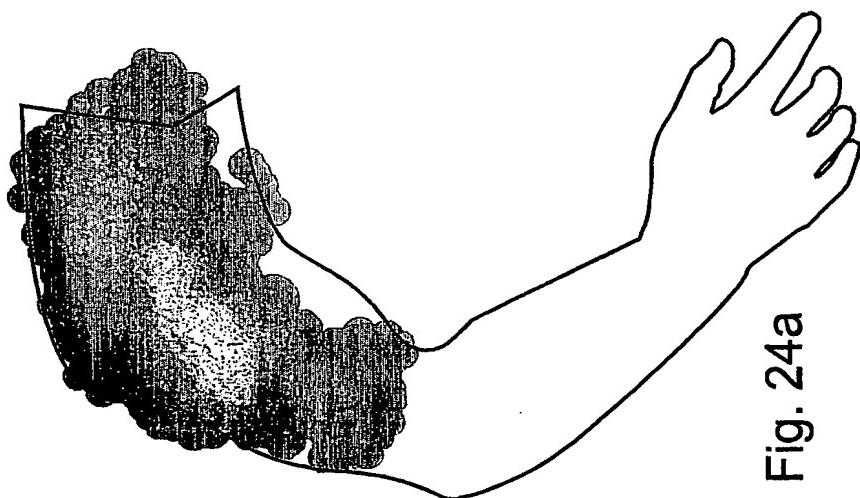


Fig. 24a

WO 02/16965

PCT/IL01/00638

JUL 2002

16/21

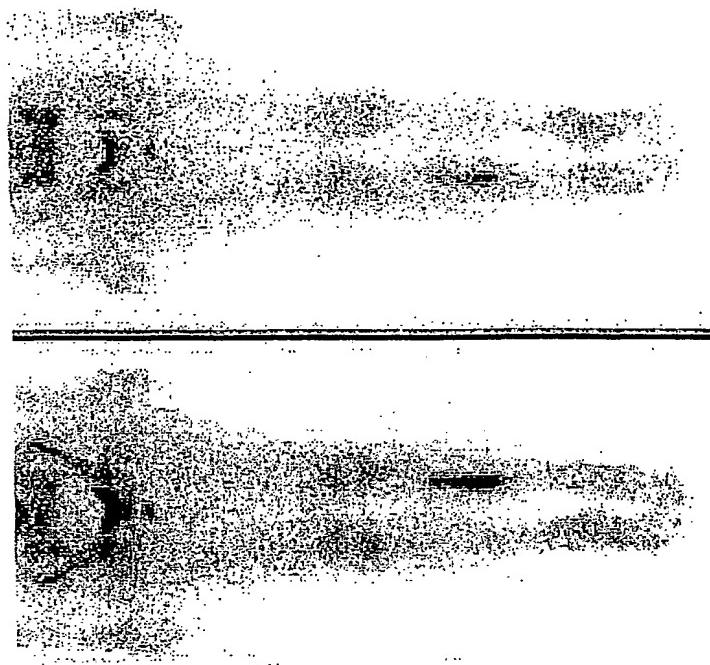


Fig. 25b

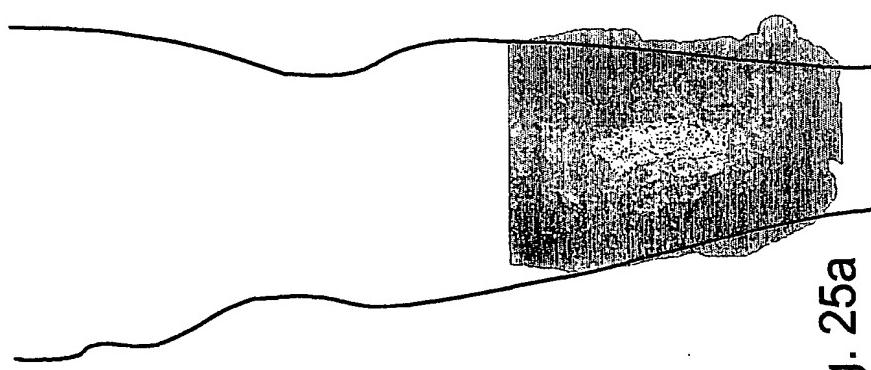


Fig. 25a

WO 02/16965

PCT/IL01/00638

30 JUL 2001

17/21



Fig. 26b

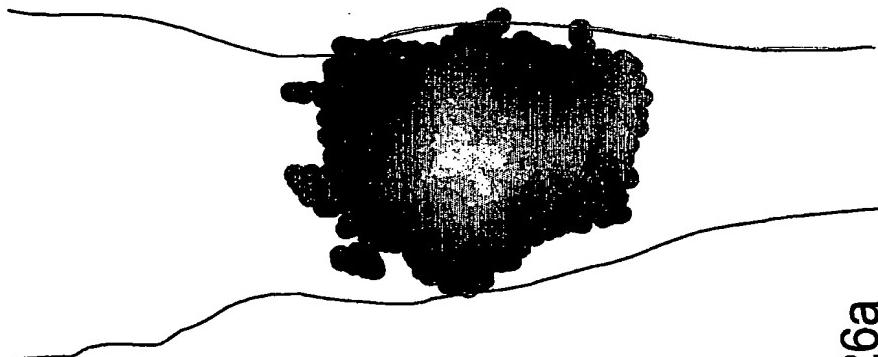


Fig. 26a

18/21

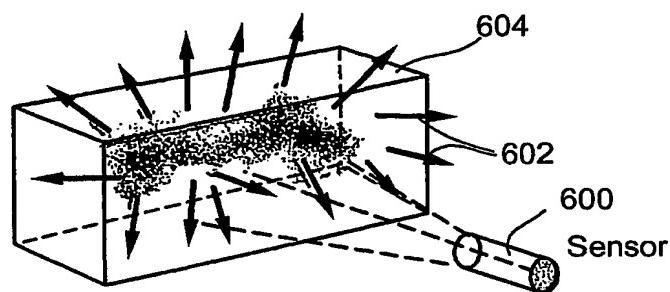


Fig. 27a

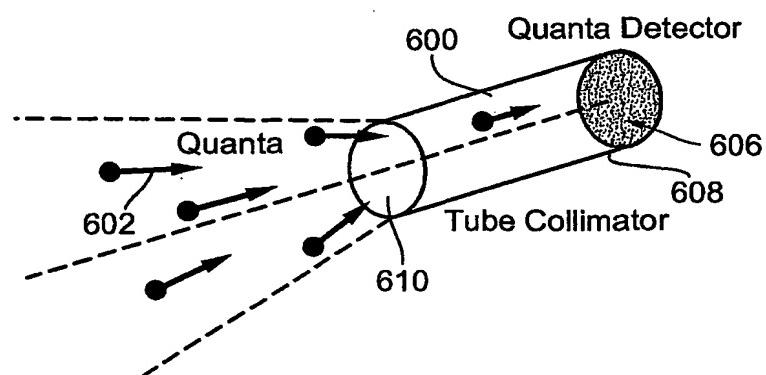


Fig. 27b

19/21

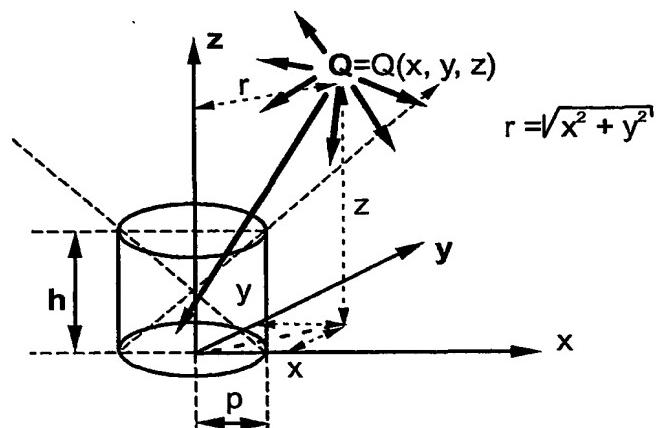


Fig. 27c

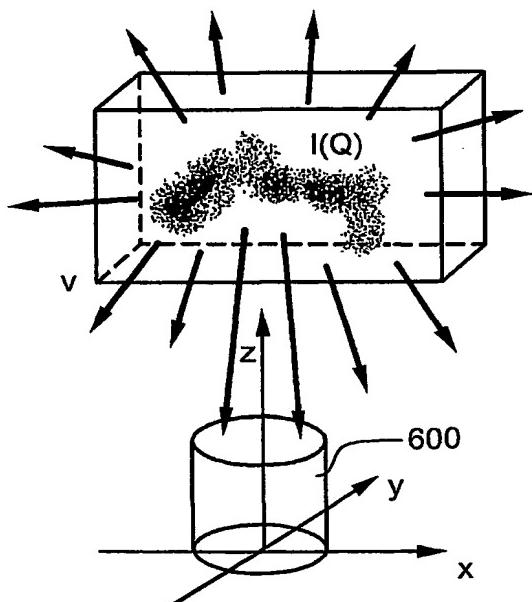


Fig. 27d

20/21

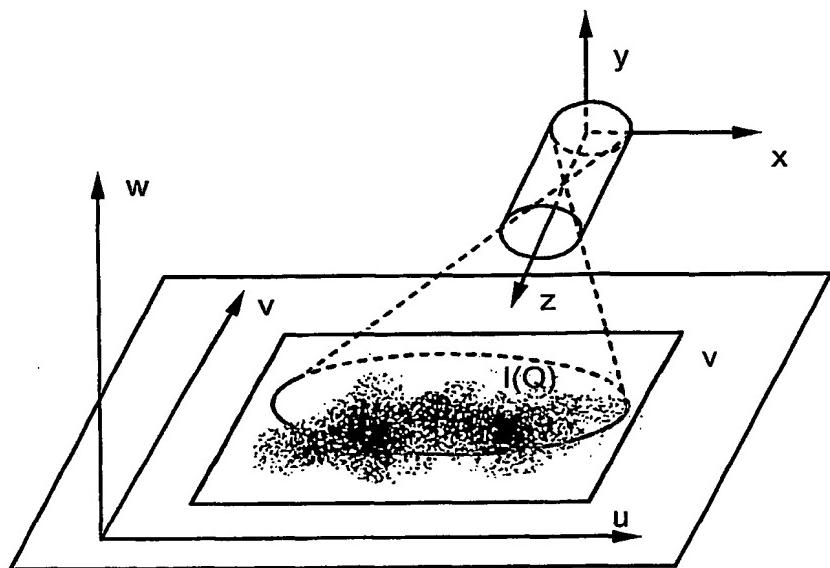


Fig. 27e

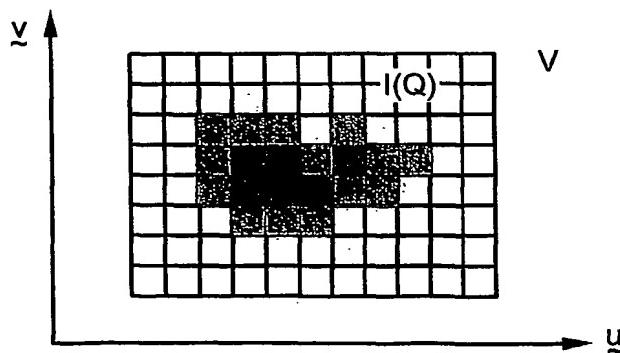
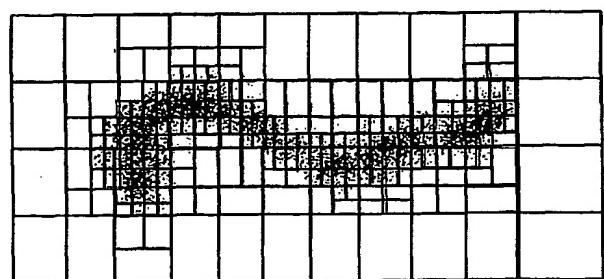


Fig. 27f

21/21



v

Fig. 27g

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number  
**WO 02/016965 A3**

(51) International Patent Classification<sup>7</sup>: **A61B 5/05**

(21) International Application Number: **PCT/IL01/00638**

(22) International Filing Date: 11 July 2001 (11.07.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

09/641,973	21 August 2000 (21.08.2000)	US
09/714,164	17 November 2000 (17.11.2000)	US
09/727,464	4 December 2000 (04.12.2000)	US
60/286,044	25 April 2001 (25.04.2001)	US

(71) Applicant (for all designated States except US): **V-TARGET LTD.** [IL/IL]; 3 Ha'etgar Street, 39120 Tirat Hacarmel (IL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KIMCHY, Yoav**

[IL/IL]; 8 Antwerpen Road, 34980 Haifa (IL). **AMRAMI, Roni** [IL/IL]; 37 Yarden Street, 20692 Yokneam (IL). **BOUSKILA, Yona** [IL/IL]; 44 Mikhmanim Street, 20106 Yokneam (IL). **ANTEBI, Udi** [IL/IL]; 30a Daphna Street, 27204 Kiryat Bialik (IL). **SIDORENKO, Nick** [IL/IL]; 4 Hamarva Street, 23393 Acre (IL). **BEN DAVID, Gal** [IL/IL]; 238 Hazait Street, 17940 Mitzpe Adi (IL). **ZILBERSTEIN, Yoel** [IL/IL]; 13 Zrubavel Street, 34671 Haifa (IL).

(74) Agent: **G. E. EHRLICH (1995) LTD.**; 28 Bezalel Street, 52521 Ramat Gan (IL).

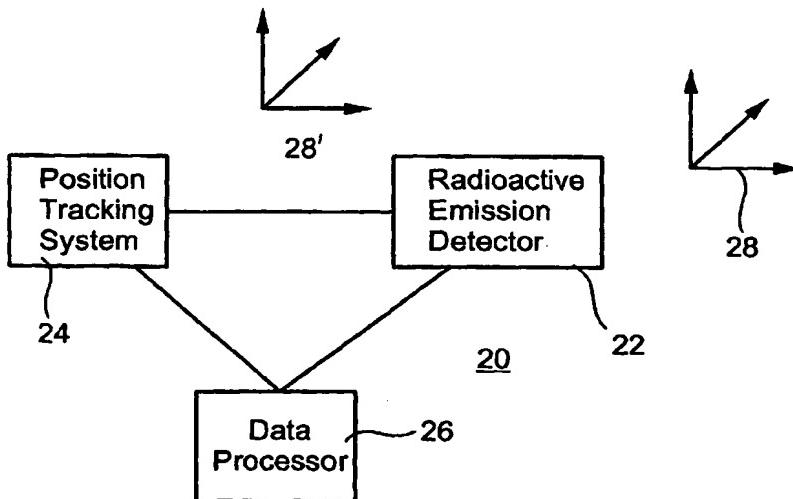
(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

*[Continued on next page]*

(54) Title: RADIOACTIVE EMISSION DETECTOR



**WO 02/016965 A3**



(57) Abstract: System (20) includes a radioactivity emission detector (22). System (20) according to the present invention further includes a position tracking system (24). System (24) is connected to and/or communicating with radioactive emission detector (22) in a two- or three-dimensional space defined by a system of co-ordinates.



(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CI, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(88) **Date of publication of the international search report:**  
6 February 2003

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**Published:**

— *with international search report*

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/IL01/00638

**A. CLASSIFICATION OF SUBJECT MATTER**

 IPC(7) : A61B 5/05  
 US CL : 600/436

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

 Minimum documentation searched (classification system followed by classification symbols)  
 U.S. : 600/407, 424, 425, 431, 436; 378/21, 41, 62, 65; 382/128; 606/130

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,493,595 A (SCHOOLMAN) 20 February 1996 (20.02.1996), see entire document.	1-254
A	US 5,727,554 A (KALEND et al) 17 March 1998 (17.03.1998), see entire document.	1-254

 Further documents are listed in the continuation of Box C.

See patent family annex.

Special categories of cited documents:	
"A"	document defining the general state of the art which is not considered to be of particular relevance
"B"	earlier application or patent published on or after the international filing date
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O"	document referring to an oral disclosure, use, exhibition or other means
"P"	document published prior to the international filing date but later than the priority date claimed
"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&"	document member of the same patent family

Date of the actual completion of the international search

23 March 2002 (23.03.2002)

Date of mailing of the international search report

21 SEP 2002

Name and mailing address of the ISA/US

 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Marvin Laiter

Telephone No. 703 308-0858

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**